```
FILE 'HOME' ENTERED AT 12:38:34 ON 23 MAY 2001
=> fil req
=> s at enolol/cn
             1 ATENOLOL/CN
=> s timolol/cn
            1 TIMOLOL/CN
L3
=> s inderal
             2 INDERAL
=> d tot
     ANSWER 1 OF 2 REGISTRY COPYRIGHT 2001 ACS
     26379-20-4 REGISTRY
RN
     Germacra-1(10),7,11-trien-15-oic acid, 8,12-epoxy-6.alpha.-hydroxy-,
CN
     .gamma.-lactone, (Z)- (8CI) (CA INDEX NAME)
OTHER NAMES:
       ***Dihydroneolinderalactone***
CN
MF
     C15 H18 O3
LC
     STN Files:
                  BEILSTEIN*, CA, CAPLUS
         (*File contains numerically searchable property data)
Currently available stereo shown.
/ Structure 1 in file .gra /
               1 REFERENCES IN FILE CA (1967 TO DATE)
               1 REFERENCES IN FILE CAPLUS (1967 TO DATE)
L5
     ANSWER 2 OF 2 REGISTRY COPYRIGHT 2001 ACS
RN
     318-98-9 REGISTRY
     2-Propanol, 1-[(1-methylethyl)amino]-3-(1-naphthalenyloxy)-, hydrochloride
CN
            (CA INDEX NAME)
OTHER CA INDEX NAMES:
     2-Propanol, 1-(isopropylamino)-3-(1-naphthyloxy)-, hydrochloride (8CI)
OTHER NAMES:
     (.+-.)-Propranolol hydrochloride
CN
CN
     (R,S)-Propranolol hydrochloride
CN
     1-(1-Naphthoxy)-2-hydroxy-3-isopropylaminopropane hydrochloride
CN
     1-(1-Naphthyloxy)-2-hydroxy-3-isopropylaminopropane hydrochloride
     1-(1-Naphthyloxy)-3-(isopropylamino)-2-propanol hydrochloride
CN
     1-(Isopropylamino)-3-(1-naphthoxy)-2-propanol hydrochloride
CN
CN
     1-(Isopropylamino)-3-(1-naphthyloxy)propan-2-ol hydrochloride
CN
     Anaprilin
CN
     Anapriline
     Avlocardyl
CN
CN
     DL-Anapriline
CN
     dl-Propranolol hydrochloride
CN
     DL-Propranolol hydrochloride
CN
     Docitan
CN
     Dociton
CN
     Duranol
     ICI 45520
CN
       ***Inderal***
CN
       ***Inderal LA***
CN
CN
     Naprilin
CN
     Obsidan
CN
     Propranolol chloride
CN
     Propranolol hydrochloride
CN
     Propraratiopharm
DR
     3506-09-0, 146874-86-4
MF
     C16 H21 N O2 . Cl H
CI
     COM
                  AGRICOLA, ANABSTR, BEILSTEIN*, BIOBUSINESS, BIOSIS,
LC
     STN Files:
       BIOTECHNO, CA, CAOLD, CAPLUS, CASREACT, CBNB, CHEMCATS, CHEMLIST, CIN,
       CSCHEM, DETHERM*, DIOGENES, DRUGPAT, EMBASE, HODOC*, HSDB*, IFICDB,
       IFIPAT, IFIUDB, IMSDIRECTORY, IPA, MRCK*, MSDS-OHS, NIOSHTIC, PHAR,
       PROMT, RTECS*, TOXLINE, TOXLIT, ULIDAT, USAN, USPATFULL
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(*File contains numerically searchable property data)
     Other Sources: EINECS**
         (**Enter CHEMLIST File for up-to-date regulatory information)
CRN
     (525-66-6)
/ Structure 2 in file .gra / .
            1758 REFERENCES IN FILE CA (1967 TO DATE)
               7 REFERENCES TO NON-SPECIFIC DERIVATIVES IN FILE CA
            1759 REFERENCES IN FILE CAPLUS (1967 TO DATE)
              30 REFERENCES IN FILE CAOLD (PRIOR TO 1967)
=> s metoprolol/cn
             1 METOPROLOL/CN
\Gamma8
=> s propranolol/cn
             1 PROPRANOLOL/CN
=> s timolol/cn
L10
            1 TIMOLOL/CN
=> s atorvastatin/cn
             1 ATORVASTATIN/CN
L11
=> s cerivastatin/cn
L12
             1 CERIVASTATIN/CN
=> s pravastatin/cn
L13
             1 PRAVASTATIN/CN
=> s fluvastatin/cn
             1 FLUVASTATIN/CN
=> s lovastatin/cn
            1 LOVASTATIN/CN
=> s simvastatin/cn
L16
             1 SIMVASTATIN/CN
=> fil medline caplus embase biosis uspatfull
=> s lll-16 or atorvastatin or cerivastatin or pravastatin or fluvastatin or lovastatin or simva
   2 FILES SEARCHED...
   4 FILES SEARCHED...
        216829 (L11 OR L12 OR L13 OR L14 OR L15 OR L16) OR ATORVASTATIN OR
               CERIVASTATIN OR PRAVASTATIN OR FLUVASTATIN OR LOVASTATIN OR
               SIMVASTATIN OR ?STATIN?
=> s 11 or 18-10 or atenolol or timolol or propranolol or metoprolol or
MISSING TERM AFTER ETOPROLOL OR
Operators must be followed by a search term, L-number, or query name.
=> s 11 or 18-10 or atended or timeled or propraneled or metoproled
        202196 L1 OR (L8 OR L9 OR L10) OR ATENOLOL OR TIMOLOL OR PROPRANOLOL
L18
               OR METOPROLOL
=> s 117 (s) 118
1,19
          1018 L17 (S) L18
=> s 117 (w) 118
L20
            28 L17 (W) L18
=> s 120 range, =2001
MISSING OPERATOR L20 RANGE, =2001
The search profile that was entered contains terms or
nested terms that are not separated by a logical operator.
=> s 120 range, = 2001
MISSING OPERATOR L20 RANGE, =
The search profile that was entered contains terms or
```

nested terms that are not separated by a logical operator. => s 120 range =, 2001 28 L20 => s 120 range =, 2000 28 L20 => d ti so tot L22 ANSWER 1 OF 28 MEDLINE Effects of sandostatin on gastric mucosal perfusion in rats with portal hypertensive gastropathy. CHUNG-HUA KAN TSANG PING TSA CHIH, (2000 Feb) 8 (1) 21-3. SO Journal code: DAU; 9710009. ISSN: 1007-3418. L22 ANSWER 2 OF 28 MEDLINE : In vitro production of angiotensin II by isolated glomeruli. TIAMERICAN JOURNAL OF PHYSIOLOGY, (1995 Feb) 268 (2 Pt 2) F266-72. SO Journal code: 3U8; 0370511. ISSN: 0002-9513. L22 ANSWER 3 OF 28 MEDLINE The effect of genetically engineered glucagon on glucose recovery after TΤ hypoglycaemia in man. BRITISH JOURNAL OF CLINICAL PHARMACOLOGY, (1992 Dec) 34 (6) 547-50. SO Journal code: AU9; 7503323. ISSN: 0306-5251. L22 ANSWER 4 OF 28 MEDLINE ጥፐ Role of hepatic autoregulation in defense against hypoglycemia in humans. JOURNAL OF CLINICAL INVESTIGATION, (1985 May) 75 (5) 1623-31. SO Journal code: HS7; 7802877. ISSN: 0021-9738. L22 ANSWER 5 OF 28 MEDLINE [Recent developments in the medical treatment of emergency cirrhotic TIhemorrhage. Vasopressin and glipressin, prostaglandins, \*\*\*somatostatin\*\*\* , \*\*\*propranolol\*\*\* , cimetidine and ranitidine]. Recenti acquisizioni in tema di trattamento medico nelle urgenze emorragiche da cirrosi. Vasopressina e glipressina, prostaglandine, somatostatina, propanololo, cimetidina e ranitidina. MINERVA MEDICA, (1983 Oct 6) 74 (38) 2189-95. SO Journal code: N6M; 0400732. ISSN: 0026-4806. L22 ANSWER 6 OF 28 CAPLUS COPYRIGHT 2001 ACS Effects of sandostatin on gastric mucosal perfusion in rats with portal ΤI hypertensive gastropathy SO Zhonghua Ganzangbing Zazhi (2000), 8(1), 21-23 CODEN: ZGZZFE; ISSN: 1007-3418 L22 ANSWER 7 OF 28 CAPLUS COPYRIGHT 2001 ACS ΤI In vitro production of angiotensin II by isolated glomeruli SO Am. J. Physiol. (1995), 268(2, Pt. 2), F266-F272 CODEN: AJPHAP; ISSN: 0002-9513 ANSWER 8 OF 28 CAPLUS COPYRIGHT 2001 ACS L22 The effect of genetically engineered glucagon on glucose recovery after hypoglycemia in man Br. J. Clin. Pharmacol. (1992), 34(6), 547-50 CODEN: BCPHBM; ISSN: 0306-5251 L22 ANSWER 9 OF 28 CAPLUS COPYRIGHT 2001 ACS Role of hepatic autoregulation in defense against hypoglycemia in humans TIJ. Clin. Invest. (1985), 75(5), 1623-31 SO CODEN: JCINAO; ISSN: 0021-9738 ANSWER 10 OF 28 EMBASE COPYRIGHT 2001 ELSEVIER SCI. B.V. L22 In vitro production of angiotensin II by isolated glomeruli. TIAmerican Journal of Physiology - Renal Fluid and Electrolyte Physiology, SO

(1995) 268/2 37-2 (F266-F272). ISSN: 0363-6127 CODEN: AJPFDM

TI

L22 ANSWER 11 OF 28 EMBASE COPYRIGHT 2001 ELSEVIER SCI. B.V.

The effect of genetically engineered glucagon on glucose recovery after

- hypoglycaemia in man.

  SO British Journal of Clinical Pharmacology, (1992) 34/6 (547-550).

  ISSN: 0306-5251 CODEN: BCPHBM
- L22 ANSWER 12 OF 28 EMBASE COPYRIGHT 2001 ELSEVIER SCI. B.V.
- TI New vasopressin regimen, \*\*\*somatostatin\*\*\* , \*\*\*propranolol\*\*\* tried for esophageal varices.
- SO Gastroenterology Endoscopy News, (1985) 36/11 (5). CODEN: GENNEY
- L22 ANSWER 13 OF 28 EMBASE COPYRIGHT 2001 ELSEVIER SCI. B.V.
- TI Role of hepatic autoregulation in defense against hypoglycemia in humans.
- SO Journal of Clinical Investigation, (1985) 75/5 (1623-1631).

CODEN: JCINAO

- L22 ANSWER 14 OF 28 EMBASE COPYRIGHT 2001 ELSEVIER SCI. B.V.
- TI [Recent developments in the emergency medical treatment of cirrhotic haemorrhages].

  RECENTI ACQUISIZIONI IN TEMA DI TRATTAMENTO MEDICO NELLE URGENZE EMORRAGICHE DA CIRROSI.
- SO Minerva Medica, (1983) 74/38 (2189-2195). CODEN: MIMEAO
- L22 ANSWER 15 OF 28 BIOSIS COPYRIGHT 2001 BIOSIS
- TI A human study of the regional jejunal effective permeability of \*\*\*fluvastatin\*\*\* , \*\*\*atenolol\*\*\* , metoprolol and antipyrine.
- Journal of Controlled Release, (1997) Vol. 46, No. 1-2, pp. 187.

  Meeting Info.: Proceedings of Controlled Release Society Ireland Special Symposium on Current Topics in Peptide Delivery Dublin, Ireland September 20-22, 1995
  ISSN: 0168-3659.
- L22 ANSWER 16 OF 28 BIOSIS COPYRIGHT 2001 BIOSIS
- TI A human study of the regional jejunal effective permeability of \*\*\*fluvastatin\*\*\* , \*\*\*atenolol\*\*\* , metoprolol and antipyrine.
- SO Pharmaceutical Research (New York), (1995) Vol. 12, No. 9 SUPPL., pp. S295.

  Meeting Info.: Annual Meeting of the American Association of
  - Meeting Info.: Annual Meeting of the American Association of Pharmaceutical Scientists Miami Beach, Florida, USA November 5-9, 1995 ISSN: 0724-8741.
- L22 ANSWER 17 OF 28 BIOSIS COPYRIGHT 2001 BIOSIS
- TI In vitro production of angiotensin II by isolated glomeruli.
- SO American Journal of Physiology, (1995) Vol. 268, No. 2 PART 2, pp. F266-F272.
  ISSN: 0002-9513.
- L22 ANSWER 18 OF 28 BIOSIS COPYRIGHT 2001 BIOSIS
- TI The effect of genetically engineered glucagon on glucose recovery after hypoglycaemia in man.
- SO British Journal of Clinical Pharmacology, (1992) Vol. 34, No. 6, pp. 547-550.
  ISSN: 0306-5251.
- L22 ANSWER 19 OF 28 BIOSIS COPYRIGHT 2001 BIOSIS
- TI BETA-ADRENERGIC MODULATION OF GROWTH HORMONE GH AUTOFEEDBACK ON SLEEP-ASSOCIATED AND PHARMACOLOGICALLY INDUCED GH SECRETION.
- SO J CLIN ENDOCRINOL METAB, (1989) 69 (6), 1187-1194. CODEN: JCEMAZ. ISSN: 0021-972X.
- L22 ANSWER 20 OF 28 BIOSIS COPYRIGHT 2001 BIOSIS
- TI ALPHA-1-ADRENERGIC STIMULATION OF IN-VITRO GROWTH HORMONE RELEASE AND CYTOSOLIC FREE CALCIUM IN RAT SOMATOTROPHS.
- SO ENDOCRINOLOGY, (1988) 122 (4), 1419-1425. CODEN: ENDOAO. ISSN: 0013-7227.
- L22 ANSWER 21 OF 28 BIOSIS COPYRIGHT 2001 BIOSIS
- TI PATHOGENESIS AND TREATMENT OF ESOPHAGEAL VARICEAL BLEEDING.
- SO Leber, Magen, Darm, (1986) 16 (4), 195-198,201-202,204-209. CODEN: LBMDAT. ISSN: 0300-8622.
- L22 ANSWER 22 OF 28 BIOSIS COPYRIGHT 2001 BIOSIS

- ΤI DRUG THERAPY FOR PORTAL HYPERTENSION.
- Ann. Intern. Med., (1986) 105 (1), 96-107. SO CODEN: AIMEAS. ISSN: 0003-4819.
- L22 ANSWER 23 OF 28 BIOSIS COPYRIGHT 2001 BIOSIS
- ROLE OF HEPATIC AUTOREGULATION IN DEFENSE AGAINST HYPOGLYCEMIA IN HUMANS. ΤI
- J CLIN INVEST, (1985) 75 (5), 1623-1631. CODEN: JCINAO. ISSN: 0021-9738. SO
- L22 ANSWER 24 OF 28 BIOSIS COPYRIGHT 2001 BIOSIS
- GLUCOSE COUNTERREGULATION DURING RECOVERY FROM NEUROGLUCOPENIA WHICH TI MECHANISM IS IMPORTANT.
- METAB CLIN EXP, (1985) 34 (1), 15-18. SO CODEN: METAAJ. ISSN: 0026-0495.
- L22 ANSWER 25 OF 28 BIOSIS COPYRIGHT 2001 BIOSIS
- PHARMACOLOGICAL MODIFICATIONS OF INSULIN RELEASE IN-VITRO FROM TΙ FUEL-RESPONSIVE TRANSPLANTABLE INSULINOMAS.
- ENDOCRINOLOGY, (1984) 115 (4), 1496-1499. SO CODEN: ENDOAO. ISSN: 0013-7227.
- L22 ANSWER 26 OF 28 BIOSIS COPYRIGHT 2001 BIOSIS
- ENERGY AND SUBSTRATE KINETICS AND OXIDATION DURING KETONE INFUSION IN ΤŢ SEPTIC DOGS ROLE OF CHANGES IN INSULIN AND GLUCAGON.
- CIRC SHOCK, (1984) 14 (1), 63-79. SO CODEN: CRSHAG. ISSN: 0092-6213.
- L22 ANSWER 27 OF 28 BIOSIS COPYRIGHT 2001 BIOSIS
- ΤI VASOPRESSIN AND VASOCONSTRICTOR THERAPY.
- SHEPHERD, A. P. AND D. N. GRANGER (ED.). PHYSIOLOGY OF THE INTESTINAL SO CIRCULATION. XIX+420P. RAVEN PRESS: NEW YORK, N.Y., USA. ILLUS. (1984) 0 (0), 377-392. ISBN: 0-88167-025-1.
- ANSWER 28 OF 28 BIOSIS COPYRIGHT 2001 BIOSIS L22
- A CASE OF INSULINOMA DIAGNOSTIC SIGNIFICANCE OF INSULIN SUPPRESSION TEST ΤI AND PRO INSULIN DETERMINATION IN INSULINOMA.
- Tonyobyo (Tokyo), (1977) 20 (4), 461-468. SO
  - CODEN: TONYA4. ISSN: 0021-437X.
- => s lll-16 or atorvastatin or cerivastatin or pravastatin or fluvastatin or lovastatin or simva 23940 (L11 OR L12 OR L13 OR L14 OR L15 OR L16) OR ATORVASTATIN OR CERIVASTATIN OR PRAVASTATIN OR FLUVASTATIN OR LOVASTATIN OR SIMVASTATIN
- $\Rightarrow$  s 123 (s) (l1 or atenolol)
- 72 L23 (S) (L1 OR ATENOLOL)
- $\Rightarrow$  s 123 (w) (11 or atenolol)
- L25 2 L23 (W) (L1 OR ATENOLOL)
- => d ibib abs tot
- L25 ANSWER 1 OF 2 BIOSIS COPYRIGHT 2001 BIOSIS
- 1997:331686 BIOSIS ACCESSION NUMBER:
- DOCUMENT NUMBER: PREV199799630889
- A human study of the regional jejunal effective TITLE:
  - permeability of \*\*\*fluvastatin\*\*\* , \*\*\*atenolol\*\*\* ,
  - metoprolol and antipyrine.
- Lindahl, A. (1); Sandstrom, R. (1); Ungell, A. L.; Knutson, AUTHOR(S):
  - L.; Abrahamsson, B.; Lennernas, H. (1)
- (1) Div. Biopharmaceutics Pharmacokinetics, Univ. Uppsala, CORPORATE SOURCE:
  - Uppsala Sweden
- SOURCE: Journal of Controlled Release, (1997) Vol. 46, No. 1-2, pp.

  - Meeting Info.: Proceedings of Controlled Release Society Ireland Special Symposium on Current Topics in Peptide
    - Delivery Dublin, Ireland September 20-22, 1995
    - ISSN: 0168-3659.
- Conference; Abstract DOCUMENT TYPE:
- English

LANGUAGE:

L25 ANSWER 2 OF 2 BIOSIS COPYRIGHT 2001 BIOSIS

ACCESSION NUMBER: 1996:3741 BIOSIS DOCUMENT NUMBER: PREV199698575876

TITLE: A human study of the regional jejunal effective

permeability of \*\*\*fluvastatin\*\*\* , \*\*\*atenolol\*\*\* ,

metoprolol and antipyrine.

AUTHOR(S): Lindahl, A. (1); Sandstrom, R. (1); Ungell, A.-L.; Knutson,

L.; Abrahamsson, B.; Lennernas, H. (1)

CORPORATE SOURCE: (1) Div. Biopharm. Pharmacokin., Univ. Uppsala, Uppsala

Sweden

SOURCE: Pharmaceutical Research (New York), (1995) Vol. 12, No. 9

SUPPL., pp. S295.

Meeting Info.: Annual Meeting of the American Association of Pharmaceutical Scientists Miami Beach, Florida, USA

November 5-9, 1995 ISSN: 0724-8741.

DOCUMENT TYPE:

LANGUAGE:

Conference English

=> s 123 (s) (13 or timolol)

L26 46 L23 (S) (L3 OR TIMOLOL)

=> s 123 (a) (13 or timolol)

L27 0 L23 (A) (L3 OR TIMOLOL)

=> s 123 (p) (13 or timolol) \*

L28 46 L23 (P) (L3 OR TIMOLOL)

=> dup rem 128

PROCESSING COMPLETED FOR L28

L29 44 DUP REM L28 (2 DUPLICATES REMOVED)

=> s 129 (s) folic acid

L30 23 L29 (S) FOLIC ACID

=> d ibib abs 1-5

L30 ANSWER 1 OF 23 USPATFULL

ACCESSION NUMBER: 2001:59392 USPATFULL

TITLE: Process for producing solid dosage forms by extrusion

INVENTOR(S): Breitenbach, Jorg, Mannheim, Germany, Federal Republic

of

Kleinke, Andreas, Ludwigshafen, Germany, Federal

Republic of

Kothrade, Stephan, Limburgerhof, Germany, Federal

Republic of

Rosenberg, Joerg, Ellerstadt, Germany, Federal Republic

οf

PATENT ASSIGNEE(S): BASF Aktiengesellschaft, Ludwigshafen, Germany, Federal

Republic of (non-U.S. corporation)

19990310 PCT 371 date 19990310 PCT 102(e) date

NUMBER DATE

PRIORITY INFORMATION: DE 1996-19637479 19960913 DE 1997-19734011 19970806

DOCUMENT TYPE: Utility

PRIMARY EXAMINER: Lankford, Jr., Leon B. LEGAL REPRESENTATIVE: Dergosits & Noah LLP

NUMBER OF CLAIMS: 16 EXEMPLARY CLAIM: 1 LINE COUNT: 669

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

A process for producing solid dose forms by mixing at least one polymeric binder, with or without at least one active ingredient and with or without conventional additives, and shaping the mixture, where at least one of the components is employed in liquid form.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

L30 ANSWER 2 OF 23 USPATFULL

ACCESSION NUMBER: 2001:25358 USPATFULL

TITLE: Embedding and encapsulation of controlled release

particles

van Lengerich, Bernhard H., Plymouth, MN, United States INVENTOR(S):

PATENT ASSIGNEE(S): General Mills, Inc., Minneapolis, MN, United States

(U.S. corporation)

NUMBER DATE -----PATENT INFORMATION: US 6190591 20010220 WO 9818610 19980507 APPLICATION INFO.: US 1999-269763 19990517 WO 1997-US18984 19971027 19990517 PCT 371 date 19990517 PCT 102(e) date

DOCUMENT TYPE: Utility

PRIMARY EXAMINER: Silbaugh, Jan H. ASSISTANT EXAMINER: Eashoo, Mark

LEGAL REPRESENTATIVE: Hollander, Barry I; O'Toole, John A.; Taylor, Douglas

J.

NUMBER OF CLAIMS: 26 EXEMPLARY CLAIM: 1

NUMBER OF DRAWINGS: 6 Drawing Figure(s); 6 Drawing Page(s)

LINE COUNT: 1778

AB Controlled release, discrete, solid particles which contain an encapsulated and/or embedded component such as a heat sensitive destruction or readily oxidizable pharnaceutically, biologically, or nutritionally active component are continuously produced without substantial destruction of the matrix or encapsulant. A release-rate controlling component is incorporated into the matrix to control the rate of release the encapsulant from the particles. the additional component may be a hydrophobic component or a high water binding capacity component for extending the release time. The plasticizable matrix material, such as starch, is admixed with at least one plasticizer, such as water, and at least one release-rate controlling component under low shear mixing conditions to plasticize the plasticizable material without substantially destroying the at least one plasticizable material and to obtain a substantially homogeneous plasticized mass. The plasticizer content is substantially reduced and the temperature of the plasticized mass is substantially reduced prior to admixing the plasticized mass with the encapsulant to avoid substantial destruction of the encapsulant and to obtain a formable, extrudable mixture. The mixture is extruded though a die without substantial or essentially no expansion and cut into discrete, relatively dense particles. Release properties may also be controlled by precoating the encapsulant and/or coating the extruded particles with a film-forming component.

L30 ANSWER 3 OF 23 USPATFULL

ACCESSION NUMBER: 2001:21790 USPATFULL

TITLE: Solid medicaments obtained by extrusion of an

isomalt-containing polymer-active substance melt

INVENTOR(S): Zeidler, Jurgen, Mutterstadt, Germany, Federal Republic

Rosenberg, Joerg, Ellerstadt, Germany, Federal Republic

Neumann, Jorg, Limburgerhof, Germany, Federal Republic

Breitenbach, Jorg, Mannheim, Germany, Federal Republic

PATENT ASSIGNEE(S): BASF Aktiengesellschaft, Ludwigshafen, Germany, Federal Republic of (non-U.S. corporation)

NUMBER DATE \_\_\_\_\_ US 6187342 20010213 WO 9712603 19970410 US 1998-29362 19980224 (9) PATENT INFORMATION: APPLICATION INFO.: WO 1996-EP4262 19960930

19980224 PCT 371 date 19980224 PCT 102(e) date

DATE NUMBER DE 1995-19536394 19950929

PRIORITY INFORMATION:

DOCUMENT TYPE: Utility
PRIMARY EXAMINER: Webman, Edward J. LEGAL REPRESENTATIVE: Keil & Weinkauf

NUMBER OF CLAIMS: 8 EXEMPLARY CLAIM: 1 406 LINE COUNT:

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

The invention relates to solid drug forms obtainable by extrusion with subsequent shaping of a solvent-free melt, comprising, besides one or more active ingredients,

A) 10-90% by weight of a melt-processable, water-soluble polymer,

B) 5-85% by weight of isomalt, and

C) 0-5% by weight of lecithin,

where the total of all the ingredients is to be equal to 100% by weight.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

L30 ANSWER 4 OF 23 USPATFULL

ACCESSION NUMBER: 2000:174141 USPATFULL

Dosage forms containing taste masked active agents TITLE:

INVENTOR(S): Mezaache, Djelila, Laurel, MD, United States

Raiden, Michael G., Corona, CA, United States Sanghvi, Pradeepkumar P., Herndon, VA, United States

Szedlock, Scott J., Sterling, VA, United States

PATENT ASSIGNEE(S): Fuisz Technologies Ltd., Chantilly, VA, United States

(U.S. corporation)

· · NUMBER - DATE

PATENT INFORMATION: US 6165512 20001226 APPLICATION INFO.: US 1998-183501 19981030 (9) APPLICATION INFO.:

NUMBER DATE \_\_\_\_\_ PRIORITY INFORMATION: US 1997-56617 19970820 (60)

DOCUMENT TYPE: Utility
PRIMARY EXAMINER: Kishore, Gollamudi S.
ASSISTANT EXAMINER: Channavajjala, Lakshmi

LEGAL REPRESENTATIVE: Levis, John F.; Schmidt, Richard D.

NUMBER OF CLAIMS: 10
EXEMPLARY CLAIM: 1 LINE COUNT: 814

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

The invention relates to compositions useful for making taste-masked AB oral dosage forms which can be easily processed and which disintegrate rapidly when placed in the mouth. The compositions include coated liquiflash particles and shearform floss particles. Tablets are preferred dosage forms.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

L30 ANSWER 5 OF 23 USPATFULL

ACCESSION NUMBER: 2000:157473 USPATFULL

TITLE: Solid foamed active substance preparations INVENTOR(S): Breitenbach, Jorg, Mannheim, Germany, Federal Republic

of

Baumgartl, Horst, Mainz, Germany, Federal Republic of BASF Aktiengesellschaft, Ludwigshafen, Germany, Federal

Republic of (non-U.S. corporation)

WO 1997-EP4550 19970821

19990301

19990301 PCT 371 date 19990301 PCT 102(e) date

NUMBER DATE

PRIORITY INFORMATION: DE 1996-19635676 19960903

DOCUMENT TYPE: Utility

PATENT ASSIGNEE(S):

PRIMARY EXAMINER: Clardy, S. Mark
ASSISTANT EXAMINER: George, Konata M.
LEGAL REPRESENTATIVE: Keil & Weinkauf

NUMBER OF CLAIMS: 9
EXEMPLARY CLAIM: 1
LINE COUNT: 390

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

AB Solid foamed active ingredient preparations based on melt-processable polymers, obtainable by extrusion of a melt of one or more polymers which comprises active ingredient and which is impregnated with a volatile, physiologically acceptable blowing agent and expanded.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

=> s 123 (S) (18 or metoprolol) L31 58 L23 (S) (L8 OR METOPROLOL)

=> dup rem 131
PROCESSING COMPLETED FOR L31

L32 48 DUP REM L31 (10 DUPLICATES REMOVED)

=> s 132 (s) (folic acid or folate or vitamin E)

L33 39 L32 (S) (FOLIC ACID OR FOLATE OR VITAMIN E)

=> s 132 (s) (folic acid or folate or vitamin B)

L34 17 L32 (S) (FOLIC ACID OR FOLATE OR VITAMIN B)

=> d ibib abs tot

L34 ANSWER 1 OF 17 USPATFULL

ACCESSION NUMBER: 2000:174799 USPATFULL

TITLE: Biodegradable polymers chain-extended by phosphates, compositions, articles and methods for making and using

the same

INVENTOR(S): Mao, Hai-Quan, Towson, MD, United States

Leong, Kam W., Ellicott City, MD, United States

Zhao, 'Zhong, Baltimore, MD, United States English, James P., Chelsea, AL, United States

PATENT ASSIGNEE(S): Guilford Pharmaceuticals Inc., Baltimore, MD, United

States (U.S. corporation)

Johns Hopkins University, Baltimore, MD, United States

(U.S. corporation)

RELATED APPLN. INFO.: Continuation-in-part of Ser. No. US 1997-832217, filed

on 3 Apr 1997, now abandoned

DOCUMENT TYPE: Utility

PRIMARY EXAMINER: Merriam, Andrew E. C.

NUMBER OF CLAIMS: ZEXEMPLARY CLAIM:

NUMBER OF DRAWINGS: 17 Drawing Figure(s); 14 Drawing Page(s)

LINE COUNT: 2164

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

Biodegradable polymers are described comprising the recurring monomeric units shown in formula I or II: wherein X is --O-- or --NR'--, where R' is H or alkyl; L is a branched or straight chain aliphatic group having from 1-20 carbon atoms; M.sub.1 and M.sub.2 are each independently (1) a branched or straight chain aliphatic group having from 1-20 carbon atoms; or (2) a branched or straight chain, oxy-, carboxy- or amino-aliphatic group having from 1-20 carbon atoms; Y is --O--, --S-- or --NR'--, where R' is H or alkyl; R is H, alkyl, alkoxy, aryl, aryloxy, heterocyclic or heterocycloxy; the molar ratio of x:y is about 1; the molar ratio n:(x or y) is between about 200:1 and 1:200; and the molar ratio q:r is between about 1:99 and 99:1; wherein said biodegradable polymer is biocompatible before and upon biodegradat.

Processes for preparing the polymers, compositions containing the polymers and biologically active substances, articles useful for implantation or injection into the body fabricated from the compositions, and methods for controllably releasing biologically active substances using the polymers, are also described.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

L34 ANSWER 2 OF 17 USPATFULL

ACCESSION NUMBER: 2000:160610 USPATFULL

TITLE: Biodegradable terephthalate polyester-poly

(phosphonate) compositions, articles, and methods of

using the same

INVENTOR(S): Mao, Hai-quan, Towson, MD, United States

Leong, Kam W., Ellicott City, MD, United States Zhao, Zhong, Ellicott City, MD, United States Dang, Wenbin, Ellicott City, MD, United States English, James P., Chelsea, AL, United States Nowotnik, David P., Kingsville, MD, United States

PATENT ASSIGNEE(S): Guilford Pharmaceuticals Inc., Baltimore, MD, United

States (U.S. corporation)

Johns Hopkins University School of Medicine, Baltimore,

MD, United States (U.S. corporation)

NUMBER DATE

PATENT INFORMATION: US 6153212 20001128

APPLICATION INFO: US 1998-165375 19981002 (9)

DOCUMENT TYPE: Utility

PRIMARY EXAMINER: Azpuru, Carlos A.

LEGAL REPRESENTATIVE: Howrey Simon Arnold & White, LLP

NUMBER OF CLAIMS: 59 EXEMPLARY CLAIM: 1

NUMBER OF DRAWINGS: 2 Drawing Figure(s); 2 Drawing Page(s)

LINE COUNT: 1448

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

AB A medical device is described comprising a biodegradable terephthalate copolymer comprising the recurring monomeric units shown in formula I below: ##STR1## wherein R is a divalent organic moiety; R' is an aliphatic, aromatic, or heterocyclic residue; x is .gtoreq.1; and n is 3-7,500, and where the biodegradable terephthalate copolymer is sufficiently pure to be biocompatible and is capable of forming biocompatible residues upon biodegradation. In addition, compositions containing the copolymers and biologically active substances, articles useful for implantation or injection into the body fabricated from the compositions, and methods for controllably releasing biologically active substances using the copolymers, are also described.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

L34 ANSWER 3 OF 17 USPATFULL

ACCESSION NUMBER: 2000:137750 USPATFULL

TITLE: Production of lenticular tablets by melt calendering

Rosenberg, Joerg, Ellerstadt, Germany, Federal Republic INVENTOR(S):

Maier, Werner, Schifferstadt, Germany, Federal Republic

Breitenbach, Jorg, Mannheim, Germany, Federal Republic

BASF Aktiengesellschaft, Ludwigshafen, Germany, Federal PATENT ASSIGNEE(S):

Republic of (non-U.S. corporation)

DATE NUMBER \_\_\_\_\_ US 6132659 WO 9619964 PATENT INFORMATION: 20001017 19960704 US 1997-860019 19970620 APPLICATION INFO.:

WO 1995-EP5119 19951222

19970620 PCT 371 date 19970620 PCT 102(e) date

(8)

NUMBER DATE \_\_\_\_\_

PRIORITY INFORMATION: DE 1994-4446467 19941223

Utility DOCUMENT TYPE:

Theisen, Mary Lynn PRIMARY EXAMINER: LEGAL REPRESENTATIVE: Keil & Weinkauf

NUMBER OF CLAIMS: 11 1 EXEMPLARY CLAIM:

5 Drawing Figure(s); 3 Drawing Page(s) NUMBER OF DRAWINGS:

LINE COUNT: 375

The present invention relates to a process for the production of lenticular tablets by melt calendering in which molding rolls with depressions in the shape of segments of an ellipsoid are used. The process according to the invention affords tablets which are easily deflashed and in which the tablet residue to be abraded when there is a displacement between the upper and lower half of the tablet is small.

L34 ANSWER 4 OF 17 USPATFULL

2000:61219 USPATFULL ACCESSION NUMBER:

Purified galactomannan as an improved pharmaceutical TITLE:

excipient

Gebert, Mark S., East Palo Alto, CA, United States INVENTOR(S):

Friend, David R., Menlo Park, CA, United States Wong, David, San Francisco, CA, United States

Parasrampuria, Jagdish, San Mateo, CA, United States

Venture Lending, A Division of Cupertino National Bank, PATENT ASSIGNEE(S):

Palo Alto, CA, United States (U.S. corporation)

DATE NUMBER

PATENT INFORMATION: US 6063402 20000516 US 1995-487605 19950607 (8)

DOCUMENT TYPE: Utility Peselev, Elli PRIMARY EXAMINER: LEGAL REPRESENTATIVE: Cooley Godward LLP

NUMBER OF CLAIMS: EXEMPLARY CLAIM:

NUMBER OF DRAWINGS: 1 Drawing Figure(s); 1 Drawing Page(s)

LINE COUNT: 993

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

Disclosed is a substantially anhydrous, powdered, galactomannan AB composition consisting essentially of a galactomannan hydrocolloid exhibiting about 50% to about 90% by weight of anhydromannose residues and about 10% to about 50% by weight anhydrogalactose residues; less than about 1% by weight of protein material and less than about 3% of other nonaqueous impurities. This material is useful for preparing pharmaceutical compositions both in the substantially anhydrous form but preferably in an anhydrated form which includes about 5-15% by weight water. The pharmaceutical compositions comprise a therapeutically effective amount of a drug, the hydrated powered gallactomannan composition and optionally other pharmaceutically-acceptable excipients. When the hydrated powdered purified glactomannan of the invention is used to form a tablet, one sees improved hardness in the tablet formed.

The pharmaceutical composition of the invention is particularly valuable for delivering a therapeutically effective drug to the colon without significant release of the drug in the upper GI tract after oral administration of the composition. Unique means to prepare the purified

galactomannan in large quantities is provided.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

L34 ANSWER 5 OF 17 USPATFULL

ACCESSION NUMBER: 2000:535 USPATFULL

Process and apparatus for the production of divisible TITLE:

tablets

Rosenberg, Joerg, Ellerstadt, Germany, Federal Republic INVENTOR(S):

Maier, Werner, Schifferstadt, Germany, Federal Republic

Fricke, Helmut, Mutterstadt, Germany, Federal Republic

Breitenbach, Jorg, Mannheim, Germany, Federal Republic

BASF Aktiengesellschaft, Ludwigshafen, Germany, Federal PATENT ASSIGNEE(S):

Republic of (non-U.S. corporation)

NUMBER DATE US 6009690 20000104 WO 9619962 19960704 PATENT INFORMATION: US 1997-849900 19970618 (8) APPLICATION INFO.: WO 1995-EP5117 19951222

19970618 PCT 371 date 19970618 PCT 102(e) date

NUMBER DATE \_\_\_\_\_\_ PRIORITY INFORMATION: DE 1994-4446470 19941223

DOCUMENT TYPE: Utility

PRIMARY EXAMINER: Silbaugh, Ian H. ASSISTANT EXAMINER: Lee, Dae Young LEGAL REPRESENTATIVE: Keil & Weinkauf

NUMBER OF CLAIMS: EXEMPLARY CLAIM:

NUMBER OF DRAWINGS: 7 Drawing Figure(s); 3 Drawing Page(s)

LINE COUNT: 481

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

A process for the production of divisible tablets by melt calendering in which two molding rolls are combined together, at least one of which has depressions with at least one bar which extends up to the surface line of the molding roll and forms a score.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

L34 ANSWER 6 OF 17 USPATFULL

ACCESSION NUMBER: 1999:170710 USPATFULL

Two-stage solution polymerization of high molecular TITLE:

weight poly(phosphoesters)

Zhao, Zhong, Ellicott City, MD, United States INVENTOR(S):

Mao, Hai-quan, Towson, MD, United States

Leong, Kam W., Ellicott City, MD, United States

Guilford Pharmaceuticals Inc., Baltimore, MD, United PATENT ASSIGNEE(S):

States (U.S. corporation)

Johns Hopkins University, Baltimore, MD, United States

(U.S. corporation)

NUMBER DATE \_\_\_\_\_\_ US 6008318 19991228 US 1998-98620 19980617 (9) PATENT INFORMATION: APPLICATION INFO.:

Continuation of Ser. No. US 1997-877624, filed on 18 RELATED APPLN. INFO.:

Jun 1997, now abandoned

DOCUMENT TYPE: Utility PRIMARY EXAMINER: Truong, Duc LEGAL REPRESENTATIVE: Howrey & Simon NUMBER OF CLAIMS: 38 EXEMPLARY CLAIM: 1

NUMBER OF DRAWINGS: 4 Drawing Figure(s); 4 Drawing Page(s)

LINE COUNT: 1244

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

AB A process for making a phosphoester polymer comprising the recurring monomeric units of formula I: ##STR1## wherein: X is --O-- or --NR"--, where R" is H or alkyl;

L is a divalent organic moiety;

R' is H, alkyl, alkoxy, aryl, aryloxy, heterocyclic, or heterocycloxy; and

n is between about 25 to 2,000,

is described. The process comprises the steps of:

(a) polymerizing in the presence of a solvent p moles of a di-XH compound having formula II:

wherein X and L are as defined above, with q moles, where p.apprxeq.q, of a phosphorodihalo compound to form a polymer of formula I, wherein n is about 12 to 1000, having a first molecular weight Mw.sub.1, wherein the solvent is present in an amount greater than about 5 ml of solvent per gram of compound of formula II;

- (b) removing at least about 25% of the solvent to form a more concentrated reaction mixture; and
- (c) further polymerizing the concentrated reaction mixture for an additional time sufficient to produce a polymer of formula I wherein n is between about 25 and 2,000, the polymer having a second molecular weight Mw.sub.2, which is significantly higher than Mw.sub.1.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

L34 ANSWER 7 OF 17 USPATFULL

ACCESSION NUMBER: 1999:110440 USPATFULL

TITLE: Solution polymerization of high molecular weight

poly(phosphoesters) in toluene

INVENTOR(S): Zhao, Zhong, Towson, MD, United States

PATENT ASSIGNEE(S): Guilford Pharmaceuticals Inc., Baltimore, MD, United

States (U.S. corporation)

NUMBER	DATE

PATENT INFORMATION: US 5952451 19990914 APPLICATION INFO.: US 1998-102813 19980623 (9)

RELATED APPLN. INFO.: Continuation-in-part of Ser. No. US 1997-884382, filed

on 27 Jun 1997

DOCUMENT TYPE: Utility

PRIMARY EXAMINER: Mosley, Terressa

LEGAL REPRESENTATIVE: Nath & Associates; Nath, Gary M.; Drost, Patricia M.

NUMBER OF CLAIMS: 46 EXEMPLARY CLAIM: 1

NUMBER OF DRAWINGS: 3 Drawing Figure(s); 3 Drawing Page(s)

LINE COUNT: 1148

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

AB A process for making a high molecular weight poly(phosphoester) composition comprising:

- (i) a biologically active substance; and
- (ii) a poly(phosphoester) with the recurring monomeric units: ##STR1## wherein X is --O-- or --NR"--, where R" is H or alkyl; L is a divalent organic moiety, with the proviso that L cannot have the formula ##STR2## R' is H, alkyl, alkoxy, aryl, aryloxy, heterocyclic, or heterocycloxy; and n is from about 25 to 2000,

is described. The process comprises the steps of:

- (a) substantially dissolving p moles of a di--XH compound in a solvent comprising more than 75% toluene at a first temperature between about -75.degree. C. and +60.degree. C. to form a reaction mixture;
- (b) while maintaining the reaction mixture at the first temperature, adding q moles, where p.apprxeq.q, of a phosphorodihalo compound;
- (c) gradually increasing said first temperature at a rate of less than about 1.5.degree. C. per minute as necessary to achieve a second temperature between about 0.degree. C. and 150.degree. C., and mixing the reaction mixture at the second temperature to form the polymer of formula I; and
- (d) isolating the polymer of formula I.
- (e) incorporating the biologically active substance into the polymer of formula I.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

L34 ANSWER 8 OF 17 USPATFULL

ACCESSION NUMBER:

1999:50718 USPATFULL

TITLE:

Production of covered tablets

INVENTOR(S):

Rosenberg, Joerg, Ellerstadt, Germany, Federal Republic

Maier, Werner, Schifferstadt, Germany, Federal Republic

Grabowski, Sven, Ludwigshafen, Germany, Federal

Republic of

Breitenbach, Jorg, Mannheim, Germany, Federal Republic

PATENT ASSIGNEE(S):

BASF Aktiengesellschaft, Ludwigshafen, Germany, Federal

Republic of (non-U.S. corporation)

	NUMBER	DATE	
			•
PATENT INFORMATION:	US 5897910	19990427	
	WO 9619963	19960704	
APPLICATION INFO.:	US 1997-860016	19970620	(8)
	WO 1995-EP5118	19951222	
		19970620	PCT 371 date
		19970620	PCT 102(e) date

- - NUMBER DATE

PRIORITY INFORMATION: DE 1994-4446468 19941223

DOCUMENT TYPE: Utility

PRIMARY EXAMINER:

Dudash, Diana

LEGAL REPRESENTATIVE: Keil & Weinkauf

NUMBER OF CLAIMS: EXEMPLARY CLAIM:

20

NUMBER OF DRAWINGS:

1 Drawing Figure(s); 1 Drawing Page(s)

LINE COUNT:

506

The present invention is a process for the production of covered tablets AB by melt calendering in which the melt containing active ingredient is introduced between two sheets of the covering material into the molding rolls.

L34 ANSWER 9 OF 17 USPATFULL

ACCESSION NUMBER:

1999:33594 USPATFULL

TITLE: INVENTOR(S):

Controlled release simvastatin delivery device Rork, Gerald S., Lawrence, KS, United States

Pipkin, James D., Lawrence, KS, United States

Merck & Co., Inc., Rahway, NJ, United States (U.S. PATENT ASSIGNEE(S):

corporation)

ŇUMBER DATE \_\_\_\_\_

PATENT INFORMATION:

US 5882682

19990316

WO 9612478 19960502 APPLICATION INFO.: US 1997-817129 19970801 (8)

WO 1995-US13693 19951019

19970801 PCT 371 date 19970801 PCT 102(e) date

RELATED APPLN. INFO.: Continuation of Ser. No. US 1994-327083, filed on 21

Oct 1994, now patented, Pat. No. US 5543154 which is a continuation-in-part of Ser. No. US 1993-118836, filed on 8 Sep 1993, now patented, Pat. No. US 5366738 which is a continuation of Ser. No. US 1992-902188, filed on 29 Jul 1992, now abandoned And a continuation-in-part of Ser. No. US 1991-815304, filed on 27 Dec 1991, now

abandoned

DOCUMENT TYPE: Utility

PRIMARY EXAMINER: Brouillette, D. Gabrielle

LEGAL REPRESENTATIVE: Quagliato, Carol S.; Winokur, Melvin

NUMBER OF CLAIMS: 28
EXEMPLARY CLAIM: 1

NUMBER OF DRAWINGS: 7 Drawing Figure(s); 7 Drawing Page(s)

LINE COUNT: 1067

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

AB Controlled delivery of a beneficial agent in a dispersion is provided using (i) a compressed core which contains the beneficial agent, a polymer which forms gelatinous microscopic particles upon hydration, and if desired, an agent to modulate the hydration; and (ii) a water insoluble coating which adheres to and surrounds the core and contains apertures which provide an area for the hydration and release of the dispersion. The release rate of the beneficial agent is a function of the number and size of the apertures in the coating.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

L34 ANSWER 10 OF 17 USPATFULL

ACCESSION NUMBER: 1998:143696 USPATFULL

TITLE: Transdermal delivery of medications using a combination

of penetration enhancers

INVENTOR(S): Grasela, John C., 4521 Saluto Ct., San Diego, CA,

United States 92130

Grasela, Joseph E., 4767 Ocean Blvd., San Diego, CA,

United States 92109

Jubenville, Robert M., 550 Washington St., San Diego,

CA, United States 92103

McCloskey, Joseph J., 1167 Cooperwood, Bloomfield

Hills, MI, United States 48302

NUMBER DATE

PATENT INFORMATION: US 5837289 19981117 APPLICATION INFO.: US 1996-685172 19960723 (8)

DOCUMENT TYPE: Utility

PRIMARY EXAMINER: Page, Thurman K.
ASSISTANT EXAMINER: Shelborne, Kathryne E.

LEGAL REPRESENTATIVE: Brown, Martin, Haller & McClain, LLP

NUMBER OF CLAIMS: 22 EXEMPLARY CLAIM: 1

NUMBER OF DRAWINGS: 1 Drawing Figure(s); 1 Drawing Page(s)

LINE COUNT: 879

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

AB A composition and procedures for its formation and administration are described, which provide for a convenient, efficacious and simple transdermal administration of medications from a topically applied cream. No transmission through a membrane is involved. The composition incorporates at least two separate penetration enhancers which function synergistically to provide for rapid but controllable transport of the medication from the cream into the skin. The use of a plurality of penetration enhancers, at least one of which facilitates the separation of medication from the cream and at least a second of which alters the structure of the outer layers of skin, particularly the stratum corneum, enhances migration of the drug through the stratum corneum.

L34 ANSWER 11 OF 17 USPATFULL

1998:115859 USPATFULL ACCESSION NUMBER:

Method for inducing crystalline state transition in TITLE:

medicinal substance

INVENTOR(S): Nakamichi, Kouichi, Shiga, Japan

> Izumi, Shougo, Kyoto, Japan Oka, Masaaki, Osaka, Japan

PATENT ASSIGNEE(S): Nippon Shinyaju Co., Ltd., Kyoto, Japan (non-U.S.

corporation)

NUMBER DATE \_\_\_\_\_\_

US 5811547 19980922 WO 9408561 19940428 PATENT INFORMATION: 19940428

US 1995-416815 19950609 (8) APPLICATION INFO.:

WO 1993-JP1469 19931013

19950609 PCT 371 date 19950609 PCT 102(e) date

Continuation-in-part of Ser. No. US 1993-129133, filed RELATED APPLN. INFO.:

on 15 Nov 1993, now patented, Pat. No. US 5456923,

issued on 10 Oct 1995

NUMBER DATE \_\_\_\_\_\_

JP 1992-303085 19921014 PRIORITY INFORMATION:

DOCUMENT TYPE: Utility

Shah, Mukund J. Wong, K. PRIMARY EXAMINER:

ASSISTANT EXAMINER:

LEGAL REPRESENTATIVE: Graham & James LLP

NUMBER OF CLAIMS: 12 EXEMPLARY CLAIM:

NUMBER OF DRAWINGS: 10 Drawing Figure(s); 5 Drawing Page(s)

LINE COUNT: 1410

AΒ This invention has for its object to provide a method of inducing a transition in crystalline state of a crystallizable medicinal substance with great ease and improved efficiency and uniformity on a high production scale. According to the invention, an extruder is used for inducing a transition from one crystalline state (.DELTA.) to another crystalline state in a crystallizable medicinal substance.

L34 ANSWER 12 OF 17 USPATFULL

ACCESSION NUMBER: 96:113644 USPATFULL

TITLE: Controlled release drug suspension delivery device

INVENTOR(S): Rork, Gerald S., Lawrence, KS, United States

Pipkin, James D., Lawrence, KS, United States

PATENT ASSIGNEE(S): Merck & Co., Inc., Rahway, NJ, United States (U.S.

corporation)

NUMBER DATE \_\_\_\_\_

US 5582838 19961210 PATENT INFORMATION: APPLICATION INFO.: US 1994-363451 19941222 (8)

DOCUMENT TYPE: Utility

Spear, James M. PRIMARY EXAMINER:

LEGAL REPRESENTATIVE: Bigley, Francis P.; Daniel, Mark R.

NUMBER OF CLAIMS: 23 EXEMPLARY CLAIM:

NUMBER OF DRAWINGS: 6 Drawing Figure(s); 4 Drawing Page(s)

876 LINE COUNT:

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

A device is disclosed for the controlled delivery of a beneficial agent, the device consisting of (i) a core comprising at least two layers, wherein at least one layer comprises a beneficial agent and a polymer which forms microscopic gel beads upon hydration and at least one layer which comprises a polymer which forms microscopic gel beads upon hydration; and (ii) an impermeable, insoluble coating which adheres to and surrounds the core and contains apertures which provide an area for the hydration and release of the microscopic gel beads.

L34 ANSWER 13 OF 17 USPATFULL

ACCESSION NUMBER:

96:70200 USPATFULL

TITLE:

Controlled release nifedipine delivery device

INVENTOR(S):

Rork, Gerald S., Lawrence, KS, United States

Pipkin, James D., Lawrence, KS, United States Merck & Co., Inc., Rahway, NJ, United States (U.S. PATENT ASSIGNEE(S):

corporation)

NUMBER DATE -----

PATENT INFORMATION:

US 5543154 19960806

APPLICATION INFO.:

US 1994-327083 19941021 (8)

RELATED APPLN. INFO.:

Continuation-in-part of Ser. No. US 1993-118836, filed on 8 Sep 1993, now patented, Pat. No. US 5366738 which

is a continuation of Ser. No. US 1992-902188, filed on

29 Jul 1992, now abandoned which is a

continuation-in-part of Ser. No. US 1991-815304, filed

on 27 Dec 1991, now abandoned

DOCUMENT TYPE:

Utility

PRIMARY EXAMINER:

Phelan, D. Gabrielle

LEGAL REPRESENTATIVE:

Bigley, Francis P.; Daniel, Mark R.

NUMBER OF CLAIMS: EXEMPLARY CLAIM:

16

NUMBER OF DRAWINGS:

7 Drawing Figure(s); 7 Drawing Page(s)

LINE COUNT:

933

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

A device for the controlled delivery of a beneficial agent as a gelatinous dispersion consisting of (i) a core which contains a beneficial agent, a polymer which forms gelatinous micoroscopic particles upon hydration and if desired an agent to modulate the hydration of the polymer; and (ii) an impermeable, insoluble coating which adheres to and surrounds the core and contains apertures which provide an area for the hydration and release of a disperson comprising gelatinous microscopic particles.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

L34 ANSWER 14 OF 17 USPATFULL

ACCESSION NUMBER:

96:43387 USPATFULL

TITLE:

Biodegradable controlled release flash flow melt-spun

delivery system

INVENTOR(S):

Fuisz, Richard C., Great Falls, VA, United States

PATENT ASSIGNEE(S):

Fuisz Technologies Ltd., Chantilly, VA, United States

(U.S. corporation)

NUMBER DATE -----

PATENT INFORMATION: APPLICATION INFO.:

US 5518730 19960521 US 1992-893238 19920603 (7)

DOCUMENT TYPE:

Utility

PRIMARY EXAMINER: LEGAL REPRESENTATIVE:

NUMBER OF DRAWINGS:

Webman, Edward J. Hoffmann & Baron

NUMBER OF CLAIMS:

28

EXEMPLARY CLAIM:

2 Drawing Figure(s); 2 Drawing Page(s)

LINE COUNT:

1072

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

Biodegradable controlled release delivery systems using melt-spun biodegradable polymers as carriers for bio-effecting agents such as pharmaceutical actives are disclosed. Oral dosage forms as well as implants are described.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

L34 ANSWER 15 OF 17 USPATFULL

ACCESSION NUMBER:

94:102004 USPATFULL

TITLE:

Controlled release drug dispersion delivery device

INVENTOR(S):

Rork, Gerald S., Lawrence, KS, United States Pipkin, James D., Lawrence, KS, United States

PATENT ASSIGNEE(S):

Merck & Co., Inc., Rahway, NJ, United States (U.S.

corporation)

NUMBER DATE -----

PATENT INFORMATION: US 5366738 19941122 US 1993-118836 19930908 APPLICATION INFO.: (8)

Continuation of Ser. No. US 1982-902188, filed on 29 RELATED APPLN. INFO.:

Jul 1982, now abandoned which is a continuation-in-part of Ser. No. US 1991-815304, filed on 27 Dec 1991, now

abandoned

DOCUMENT TYPE: Utility

Phelan, D. Gabrielle PRIMARY EXAMINER:

LEGAL REPRESENTATIVE: Bigley, Francis P.; Daniel, Mark R.; DiPrima, Joseph F. NUMBER OF CLAIMS: 18

NUMBER OF CLAIMS: EXEMPLARY CLAIM: 1

NUMBER OF DRAWINGS: 7 Drawing Figure(s); 7 Drawing Page(s)

LINE COUNT: 887

particles.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

A device for the controlled delivery of a beneficial agent as a gelatinous dispersion consisting of (i) a core which contains a beneficial agent, a polymer which forms gelatinous microscopic particles upon hydration and if desired an agent to modulate the hydration of the polymer; and (ii) an impermeable, insoluble coating which adheres to and surrounds the core and contains apertures which provide an area for the hydration and release of a dispersion comprising gelatinous microscopic

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

L34 ANSWER 16 OF 17 USPATFULL

94:84**0**91 USPATFULL ACCESSION NUMBER:

Spheronization process using charged resins TITLE:

McClelland, Gregory A., Lawrence, KS, United States INVENTOR(S):

Zentner, Gaylen M., Lawrence, KS, United States Merck & Co., Inc., Rahway, NJ, United States (U.S. PATENT ASSIGNEE(S):

corporation)

NUMBER DATE

PATENT INFORMATION: APPLICATION INFO.: US 5350584 19940927 US 1992-906226 19920626 (7)

Utility

DOCUMENT TYPE: Utility
PRIMARY EXAMINER: Page, Thurman K.
ASSISTANT EXAMINER: Kulkosky, Peter F.

LEGAL REPRESENTATIVE: Bigley, Francis P.; Daniel, Mark R.; DiPrima, Joseph F.

NUMBER OF CLAIMS: -EXEMPLARY CLAIM: 1 LINE COUNT: 468

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

The invention comprises a novel process for the spheronization of charged resins. Spherical multiparticlates are produced which range in size from 0.3 mm to 3 mm in diameter. The spherical particle product is microcrystalline-free. The process consists of the steps of mixing followed by wet granulation, spheronization and drying.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

L34 ANSWER 17 OF 17 USPATFULL

ACCESSION NUMBER: 93:89448 USPATFULL

TITLE: Process for producing a tablet core aperture INVENTOR(S): Appel, Leah E., Lawrence, KS, United States Zentner, Gaylen M., Lawrence, KS, United States

Merck & Co., Inc., Rahway, NJ, United States (U.S. PATENT ASSIGNEE(S):

corporation)

NUMBER DATE US 5256440 19931026 US 1992-902187 19920622 (7) PATENT INFORMATION:

APPLICATION INFO.: DOCUMENT TYPE: Utility

PRIMARY EXAMINER: PRIMARY EXAMINER:
ASSISTANT EXAMINER: Owens, Terry J. Cameron, Erma

Bigley, Francis P.; DiPrima, Joseph F. LEGAL REPRESENTATIVE:

NUMBER OF CLAIMS: 17 EXEMPLARY CLAIM: 1

3 Drawing Figure(s); 3 Drawing Page(s) NUMBER OF DRAWINGS:

502 LINE COUNT:

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

Process for preparing and film coating a dosage form. An intagliated dosage form core is produced by inscribing one or more areas on the surface of the dosage form core prior to coating. An aqueous dispersion of a polymeric coating is then applied to the intagliated dosage form core. When placed in an environment of use, the film coating within the circumscribed region of the dosage form surface is reproducibly expelled, leaving a coated core tablet with a predefined aperture in the coating which exposes a discrete portion of the core surface to the environment of use.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

=> s 123 (S) (19 or propranolol) 64 L23 (S) (L9 OR PROPRANOLOL)

=> s 135 (S) (folic acid or folate or vitamin b) 16 L35 (S) (FOLIC ACID OR FOLATE OR VITAMIN B)

=> dup rem 136 PROCESSING COMPLETED FOR L36

L37 16 DUP REM L36 (O DUPLICATES REMOVED)

=> d ibib abs kwic tot

L37 ANSWER 1 OF 16 USPATFULL

ACCESSION NUMBER: 2000:174799 USPATFULL

TITLE: Biodegradable polymers chain-extended by phosphates,

compositions, articles and methods for making and using

the same

Mao, Hai-Quan, Towson, MD, United States INVENTOR(S):

Leong, Kam W., Ellicott City, MD, United States

Zhao, Zhong, Baltimore, MD, United States English, James P., Chelsea, AL, United States

Guilford Pharmaceuticals Inc., Baltimore, MD, United PATENT ASSIGNEE(S):

States (U.S. corporation)

Johns Hopkins University, Baltimore, MD, United States

(U.S. corporation)

NUMBER DATE -----

US 6166173 20001226 US 1998-53649 19980402 (9) PATENT INFORMATION:

APPLICATION INFO.:

Continuation-in-part of Ser. No. US 1997-832217, filed RELATED APPLN. INFO.:

on 3 Apr 1997, now abandoned

DOCUMENT TYPE: Utility

PRIMARY EXAMINER: Merriam, Andrew E. C.

NUMBER OF CLAIMS: 260 EXEMPLARY CLAIM:

NUMBER OF DRAWINGS: 17 Drawing Figure(s); 14 Drawing Page(s)

LINE COUNT: 2164

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

AB Biodegradable polymers are described comprising the recurring monomeric units shown in formula I or II: wherein X is --O-- or --NR'--, where R' is H or alkyl; L is a branched or straight chain aliphatic group having from 1-20 carbon atoms) M.sub.1 and M.sub.2 are each independently (1) a branched or straight chain aliphatic group having from 1-20 carbon atoms; or (2) a branched or straight chain, oxy-, carboxy- or amino-aliphatic group having from 1-20 carbon atoms; Y is --O--, --S-or --NR'--, where R' is H or alkyl; R is H, alkyl, alkoxy, aryl, aryloxy, heterocyclic or heterocycloxy; the molar ratio of x:y is about 1; the molar ratio n:(x or y) is between about 200:1 and 1:200; and the molar ratio q:r is between about 1:99 and 99:1; wherein said biodegradable polymer is biocompatible before and upon biodegradat.

Processes for preparing the polymers, compositions containing the polymers and biologically active substances, articles useful for implantation or injection into the body fabricated from the

compositions, and methods for controllably releasing biologically active substances using the polymers, are also described.

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CAS INDEXING IS AVAILABLE FOR THIS PATENT.
      . . . albuterol and dobutamine; (36) cardiovascular agents, such as
DETD
      aspirin (ASA) (enteric coated ASA); (37) .beta.-blocker antianginals,
      such as atenolol and ***propranolol*** ; (38) calcium-channel blocker
      antianginals, such as nifedipine and verapamil; (39) nitrate
      antianginals, such as isosorbide dinitrate (ISDN); (40) cardiac
      glycoside. . . (41) class I antiarrhythmics, such as lidocaine,
      mexiletine, phenytoin, procainamide, and quinidine; (42) class II
      antiarrhythmics, such as atenolol, metoprolol, ***propranolol***
      and timolol; (43) class III antiarrhythmics, such as amiodarone; (44)
      class IV antiarrhythmics, such as diltiazem and verapamil; (45)
       .alpha.-blocker. . . angiotensin-converting enzyme inhibitor (ACE
      inhibitor) antihypertensives, such as captopril and enalapril; (47)
      .beta.-blocker antihypertensives, such as atenolol, metoprolol, nadolol,
            ***propranolol*** ; (48) calcium-channel blocker antihypertensive
      agents, such as diltiazem and nifedipine; (49) central-acting adrenergic
      antihypertensives, such as clonidine and methyldopa; (50). . . such
      as gemfibrozil and probucol; (53) bile acid sequestrant antilipemics,
      such as cholestyramine; (54) HMG-CoA reductase inhibitor antilipemics,
                ***lovastatin*** and ***pravastatin***; (55) inotropes,
      such as amrinone, dobutamine, and dopamine; (56) cardiac glycoside
      inotropes, such as digoxin; (57) thrombolytic agents, such as.
      naltrexone, and nicotine; (125) withdrawal substance abuse agents, such
      as bromocriptine; (126) minerals, such as iron, calcium, and magnesium;
             (127)
                       ***B*** .sub.12) and niacin ( ***vitamin***
        ***vitamin***
        ***B*** .sub.3); (128) vitamin C compounds, such as ascorbic acid; and
       (129) vitamin D compounds, such as calcitriol.
L37 ANSWER 2 OF 16 USPATFULL
                       2000:160610 USPATFULL
ACCESSION NUMBER:
                       Biodegradable terephthalate polyester-poly
TITLE:
                       (phosphonate) compositions, articles, and methods of
                       using the same
                       Mao, Hai-quan, Towson, MD, United States
INVENTOR(S):
                       Leong, Kam W., Ellicott City, MD, United States
                       Zhao, Zhong, Ellicott City, MD, United States
                       Dang, Wenbin, Ellicott City, MD, United States
                       English, James P., Chelsea, AL, United States
                       Nowotnik, David P., Kingsville, MD, United States
                       Guilford Pharmaceuticals Inc., Baltimore, MD, United
PATENT ASSIGNEE(S):
                       States (U.S. corporation)
                       Johns Hopkins University School of Medicine, Baltimore,
                       MD, United States (U.S. corporation)
                                         DATE
                            NUMBER
                       _____
                       US 6153212
                                       20001128
PATENT INFORMATION:
APPLICATION INFO.:
                       US 1998-165375 19981002 (9)
                       Utility
DOCUMENT TYPE:
                       Azpuru, Carlos A.
PRIMARY EXAMINER:
                       Howrey Simon Arnold & White, LLP
LEGAL REPRESENTATIVE:
                       59
NUMBER OF CLAIMS:
EXEMPLARY CLAIM:
NUMBER OF DRAWINGS:
                       2 Drawing Figure(s); 2 Drawing Page(s)
LINE COUNT:
                       1448
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
       A medical device is described comprising a biodegradable terephthalate
AΒ
       copolymer comprising the recurring monomeric units shown in formula I
       below: ##STR1## wherein R is a divalent organic moiety; R' is an
       aliphatic, aromatic, or heterocyclic residue; x is .gtoreq.1; and n is
       3-7,500, and where the biodegradable terephthalate copolymer is
       sufficiently pure to be biocompatible and is capable of forming
       biocompatible residues upon biodegradation. In addition, compositions
       containing the copolymers and biologically active substances, articles
       useful for implantation or injection into the body fabricated from the
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compositions, and methods for controllably releasing biologically active

substances using the copolymers, are also described.

CAS INDEXING IS AVAILABLE FOR THIS PATENT. . . . albuterol and dobutamine; (36) cardiovascular agents, such as aspirin (ASA) (enteric coated ASA); (37) .beta.-blocker antianginals, such as atenolol and \*\*\*propranolol\*\*\*; (38) calcium-channel blocker anti-anginals, such as nifedipine and verapamil; (39) nitrate antianginals, such as isosorbide dinitrate (ISDN); (40) cardiac glycoside. . . (41) class I antiarrhythmics, such as lidocaine, mexiletine, phenytoin, procainamide, and quinidine; (42) class II antiarrhythmics, such as atenolol, metoprolol, \*\*\*propranolol\*\*\* and timolol; (43) class III antiarrhythmics, such as amiodarone; (44) class IV antiarrhythmics, such as diltiazem and verapamil; (45) .alpha.-blocker. . . such as gemfibrozil and probucol; (53) bile acid sequestrant anti-lipemics, such as cholestyramine; (54) HMG-COA reductase inhibitor anti-lipemics, such as \*\*\*lovastatin\*\*\* \*\*\*pravastatin\*\*\* ; (55) inotropes, such as amrinone, dobutamine, and dopamine; (56) cardiac glycoside inotropes, such as digoxin; (57) thrombolytic agents, such as. . . naltrexone, and nicotine; (125) withdrawal substance abuse agents, such as bromocriptine; (126) minerals, such as iron; calcium, and magnesium; (127) \*\*\*vitamin\*\*\* compounds, such as cyano-cobalamin ( \*\*\*vitamin\*\*\* (128) vitamin C compounds, such as ascorbic acid; and (129) vitamin D compounds, such as calcitriol. ACCESSION NUMBER: 2000:137750 USPATFULL TITLE: Production of lenticular tablets by melt calendering INVENTOR(S): Rosenberg, Joerg, Ellerstadt, Germany, Federal Republic Maier, Werner, Schifferstadt, Germany, Federal Republic

#### L37 ANSWER 3 OF 16 USPATFULL

Breitenbach, Jorg, Mannheim, Germany, Federal Republic

BASF Aktiengesellschaft, Ludwigshafen, Germany, Federal PATENT ASSIGNEE(S):

Republic of (non-U.S. corporation)

NUMBER DATE \_\_\_\_\_ US 6132659 20001017 WO 9619964 19960704 PATENT INFORMATION: US 1997-860019 19970620 (8) APPLICATION INFO.: WO 1995-EP5119 19951222 19970620 PCT 371 date

19970620 PCT 102(e) date

NUMBER DATE

PRIORITY INFORMATION: DE 1994-4446467 19941223

DOCUMENT TYPE: Utility

Theisen, Mary Lynn PRIMARY EXAMINER: LEGAL REPRESENTATIVE: Keil & Weinkauf

NUMBER OF CLAIMS: 11 EXEMPLARY CLAIM:

5 Drawing Figure(s); 3 Drawing Page(s) NUMBER OF DRAWINGS:

LINE COUNT: 375

AB The present invention relates to a process for the production of lenticular tablets by melt calendering in which molding rolls with depressions in the shape of segments of an ellipsoid are used. The process according to the invention affords tablets which are easily deflashed and in which the tablet residue to be abraded when there is a displacement between the upper and lower half of the tablet is small.

DETD . . . isotretinoin, ketotifen, ketoconazole, ketoprofen, ketorolac, labetalol, lactulose, lecithin, levocarnitine, levodopa, levoglutamide, levonorgestrel, levothyroxine, lidocaine, lipase, lipoic acid, lisinopril, loperamide, lorazepam, \*\*\*lovastatin\*\*\* , medroxyprogesterone, menthol, methotrexate, methyldopa, methylprednisolone, metoclopramide, metoprolol, miconazole, midazolam, minocycline, minoxidil, misoprostol, morphine, multivitamin mixtures or combinations and mineral salts,. . . omeprazole, ondansetron, pancreatin, panthenol, pantothenic acid, paracetamol, penicillin G, penicillin V, phenobarbital, pentoxifylline, phenylephrine,

phenylpropanolamine, phenytoin, piroxicam, polymyxin B, povidone-iodine, \*\*\*pravastatin\*\*\* , prednisolone, bromocriptine, propafenone,
\*\*\*propranolol\*\*\* , pseudoephedrine, pyridoxine, quinidine, ramipril, ranitidine, reserpine, retinol, riboflavin, rifampicin, rutoside, \*\*\*simvastatin\*\*\* saccharin, salbutamol, salcatonin, salicylic acid, , somatropin, sotalol, spironolactone, sucralfate, sulbactam, sulfamethoxazole, sulpiride, tamoxifen, tegafur, teprenon, terazosin, terbutaline, terfenadine, theophylline, thiamine, ticlopidine, timolol, tranexamic acid, tretihoin, triamcinolone acetonide, triamteren, trimethoprim, troxerutin, uracil, valproic acid, vancomycin, verapamil, D.sub.3, E, K, folinic acid, zidovudine.

L37 ANSWER 4 OF 16 USPATFULL

ACCESSION NUMBER: 2000:61219 USPATFULL

TITLE: Purified galactomannan as an improved pharmaceutical

excipient

INVENTOR(S): Gebert, Mark S., East Palo Alto, CA, United States

> Friend, David R., Menlo Park, CA, United States Wong, David, San Francisco, CA, United States

Parasrampuria, Jagdish, San Mateo, CA, United States

PATENT ASSIGNEE(S): Venture Lending, A Division of Cupertino National Bank,

Palo Alto, CA, United States (U.S. corporation)

NUMBER DATE -----

US 6063402 PATENT INFORMATION:

20000516 US 1995-487605 19950607 (8) APPLICATION INFO.:

Utiliţy DOCUMENT TYPE:

PRIMARY EXAMINER: Peselev, Elli LEGAL REPRESENTATIVE: Cooley Godward LLP

NUMBER OF CLAIMS: EXEMPLARY CLAIM:

NUMBER OF DRAWINGS: 1 Drawing Figure(s); 1 Drawing Page(s)

LINE COUNT:

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

Disclosed is a substantially anhydrous, powdered, galactomannan composition consisting essentially of a galactomannan hydrocolloid exhibiting about 50% to about 90% by weight of anhydromannose residues and about 10% to about 50% by weight anhydrogalactose residues; less than about 1% by weight of protein material and less than about 3% of other nonaqueous impurities. This material is useful for preparing pharmaceutical compositions both in the substantially anhydrous form but preferably in an anhydrated form which includes about 5-15% by weight water. The pharmaceutical compositions comprise a therapeutically effective amount of a drug, the hydrated powered gallactomannan composition and optionally other pharmaceutically-acceptable excipients. When the hydrated powdered purified glactomannan of the invention is used to form a tablet, one sees improved hardness in the tablet formed. The pharmaceutical composition of the invention is particularly valuable for delivering a therapeutically effective drug to the colon without significant release of the drug in the upper GI tract after oral administration of the composition. Unique means to prepare the purified galactomannan in large quantities is provided.

# CAS INDEXING IS AVAILABLE FOR THIS PATENT.

DETD . . . such as phenylpropanolamine hydrochloride; stimulants, such as caffeine; water soluble and fat soluble vitamins or precursors, such as vitamin C, \*\*\*vitamin\*\*\* \*\*\*B\*\*\* -12, tocopherol, vitamin D, vitamin A, .beta.-carotene, etc.; antihypercholesterolemics, such as Gemfibrozil and \*\*\*lovastatin\*\*\* ; antitussives, such as dextromethorphan and its hydrobromide, noscapine, carbetapentane citrate, and chlophedianol hydrochloride; antihistamines, such as chlorpheniramine maleate, phenidamine tartrate, . . . doxylamine succinate, and phenyltoloxamine citrate; decongestants, such as phenylephrine hydrochloride, phenylpropanolamine hydrochloride, pseudoephedrine hydrochloride, ephedrine; .beta.-adrenergic receptor antagonists (such as \*\*\*propranolol\*\*\* , nadalol, timolol, pindolol, labetalol, metoprolol, atenolol, esniolol, and acebutolol). Using such compounds, the compositions of this invention are adjusted to. . .

ACCESSION NUMBER: 2000:535 USPATFULL TITLE: Process and apparatus for the production of divisible INVENTOR(S): Rosenberg, Joerg, Ellerstadt, Germany, Federal Republic Maier, Werner, Schifferstadt, Germany, Federal Republic Fricke, Helmut, Mutterstadt, Germany, Federal Republic Breitenbach, Jorg, Mannheim, Germany, Federal Republic PATENT ASSIGNEE(S): BASF Aktiengesellschaft, Ludwigshafen, Germany, Federal Republic of (non-U.S. corporation) NUMBER DATE -----PATENT INFORMATION: US 6009690 20000104 WO 9619962 19960704 APPLICATION INFO.: US 1997-849900 19970618 19951222 WO 1995-EP5117 19970618 PCT 371 date 19970618 PCT 102(e) date NUMBER DATE \_\_\_\_\_ PRIORITY INFORMATION: DE 1994-4446470 19941223 DOCUMENT TYPE: Utility PRIMARY EXAMINER:

ASSISTANT EXAMINER:

Silbaugh, Ian H. Lee, Dae Young LEGAL REPRESENTATIVE: Keil & Weinkauf

NUMBER OF CLAIMS: EXEMPLARY CLAIM:

NUMBER OF DRAWINGS:

7 Drawing Figure(s); 3 Drawing Page(s)

LINE COUNT:

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

481

AΒ A process for the production of divisible tablets by melt calendering in which two molding rolls are combined together, at least one of which has depressions with at least one bar which extends up to the surface line of the molding roll and forms a score.

# CAS INDEXING IS AVAILABLE FOR THIS PATENT.

SUMM . . . isotretinoin, ketotifen, ketoconazole, ketoprofen, ketorolac, labetalol, lactulose, lecithin, levocarnitine, levodopa, levoglutamide, levonorgestrel, levothyroxine, lidocaine, lipase, lipoic acid, lisinopril, loperamide, lorazepam, \*\*\*lovastatin\*\*\* medroxyprogesterone, menthol, methotrexate, methyldopa, methylprednisolone, metoclopramide, metoprolol, miconazole, midazolam, minocycline, minoxidil, misoprostol, morphine, multivitamin mixtures or combinations and mineral salts,. . . omeprazole, ondansetron, pancreatin, panthenol, pantothenic acid, paracetamol, penicillin G, penicillin V, phenobarbital, pentoxifylline, phenylephrine, phenylpropanolamine, phenytoin, piroxicam, polymyxin B, povidone-iodine, \*\*\*pravastatin\*\*\* , prednisolone, bromocriptine, propafenone, 
\*\*\*propranolol\*\*\* , pseudoephedrine, pyridoxine, quinidine, ramipril, ranitidine, reserpine, retinol, riboflavin, rifampicin, rutoside, saccharin, salbutamol, salcatonin, salicylic acid, \*\*\*simvastatin\*\*\* , somatropin, sotalol, spironolactone, sucralfate, sulbactam, sulfamethoxazole, sulpiride, tamoxifen, tegafur, teprenone, terazosin, terbutaline, terfenadine, theophylline, thiamine, ticlopidine, timolol, tranexamic acid, tretinoin, triamcinolone acetonide, triamterene, trimethoprim, troxerutin, uracil, valproic acid, vancomycin, verapamil, \*\*\*vitamins\*\*\* \*\*\*B\*\*\* .sub.1, B.sub.2, B.sub.4, B.sub.6, B.sub.12, D.sub.3, E, K, folinic acid, zidovudine.

#### L37 ANSWER 6 OF 16 USPATFULL

ACCESSION NUMBER: 1999:170710 USPATFULL

TITLE:

Two-stage solution polymerization of high molecular

weight poly(phosphoesters)

INVENTOR(S): Zhao, Zhong, Ellicott City, MD, United States

Leong, Kam W., Ellicott City, MD, United States

Mao, Hai-quan, Towson, MD, United States

PATENT ASSIGNEE(S): Guilford Pharmaceuticals Inc., Baltimore, MD, United States (U.S. corporation)
Johns Hopkins University, Baltimore, MD, United States
(U.S. corporation)

NUMBER DATE

PATENT INFORMATION: US

US 6008318 19991228 US 1998-98620 19980617 (9)

APPLICATION INFO.: US 1998-98620 19980617 (9)

RELATED APPLN. INFO.: Continuation of Ser. No. US 1997-877624, filed on 18

Jun 1997, now abandoned

DOCUMENT TYPE: Utility
PRIMARY EXAMINER: Truong, Duc
LEGAL REPRESENTATIVE: Howrey & Simon

NUMBER OF CLAIMS: 38 EXEMPLARY CLAIM: 1

NUMBER OF DRAWINGS: 4 Drawing Figure(s); 4 Drawing Page(s)

LINE COUNT: 1244

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

AB A process for making a phosphoester polymer comprising the recurring monomeric units of formula I: ##STR1## wherein: X is --O-- or --NR"--, where R" is H or alkyl;

L is a divalent organic moiety;

R' is H, alkyl, alkoxy, aryl, aryloxy, heterocyclic, or heterocycloxy; and

n is between about 25 to 2,000,

is described. The process comprises the steps of:

(a) polymerizing in the presence of a solvent p moles of a di-XH compound having formula II:

H--X--F-X--H

wherein X and L are as defined above, with q moles, where p.apprxeq.q, of a phosphorodihalo compound to form a polymer of formula I, wherein n is about 12 to 1000, having a first molecular weight Mw.sub.1, wherein the solvent is present in an amount greater than about 5 ml of solvent per gram of compound of formula II;

- (b) removing at least about 25% of the solvent to form a more concentrated reaction mixture; and
- (c) further polymerizing the concentrated reaction mixture for an additional time sufficient to produce a polymer of formula I wherein n is between about 25 and 2,000, the polymer having a second molecular weight Mw.sub.2, which is significantly higher than Mw.sub.1.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

DETD . . . albuterol and dobutamine:

. . . albuterol and dobutamine; (36) cardiovascular agents, such as aspirin (ASA) (enteric coated ASA); (37) .beta.-blocker antianginals, such as atenolol and \*\*\*propranolol\*\*\*; (38) calcium-channel blocker antianginals, such as nifedipine and verapamil; (39) nitrate antianginals, such as isosorbide dinitrate (ISDN); (40) cardiac glycoside. . . (41) class I antiarrhythmics, such as lidocaine, mexiletine, phenytoin, procainamide, and quinidine; (42) class II antiarrhythmics, such as atenolol, metoprolol, \*\*\*propranolol\*\*\* and timolol; (43) class III antiarrhythmics, such as amiodarone; (44) class IV antiarrhythmics, such as diltiazem and verapamil; (45) .alpha.-blocker. . . such as gemfibrozil and probucol; (53) bile acid sequestrant antilipemics, such as cholestyramine; (54) HMG-CoA reductase inhibitor antilipemics, such as \*\*\*lovastatin\*\*\* and

\*\*\*pravastatin\*\*\* ; (55) inotropes, such as amrinone, dobutamine, and dopamine; (56) cardiac glycoside inotropes, such as digoxin; (57) thrombolytic agents, such as. . . naltrexone, and nicotine; (125) withdrawal substance abuse agents, such as bromocriptine; (126) minerals, such as iron, calcium, and magnesium; (127) \*\*\*vitamin\*\*\*

\*\*\*B\*\*\* compounds, such as cyanocobalamin ( \*\*\*vitamin\*\*\* \*\*\*B\*\*\*
.sub.12) and niacin ( \*\*\*vitamin\*\*\* \*\*\*B\*\*\* .sub.3); (128) vitamin

C compounds, such as ascorbic acid; and (129) vitamin D compounds, such

as calcitriol.

L37 ANSWER 7 OF 16 USPATFULL

ACCESSION NUMBER: 1999:110440 USPATFULL

TITLE: Solution polymerization of high molecular weight

poly(phosphoesters) in toluene

INVENTOR(S): Zhao, Zhong, Towson, MD, United States

PATENT ASSIGNEE(S): Guilford Pharmaceuticals Inc., Baltimore, MD, United

States (U.S. corporation)

NUMBER DATE -----

PATENT INFORMATION: US 5952451 19990914

APPLICATION INFO.: US 1998-102813 19980623 (9)

RELATED APPLN. INFO.: Continuation-in-part of Ser. No. US 1997-884382, filed

on 27 Jun 1997

DOCUMENT TYPE: Utility

Mosley, Terressa PRIMARY EXAMINER:

LEGAL REPRESENTATIVE: Nath & Associates; Nath, Gary M.; Drost, Patricia M.

NUMBER OF CLAIMS: 46

EXEMPLARY CLAIM: 1

NUMBER OF DRAWINGS: 3 Drawing Figure(s); 3 Drawing Page(s)

LINE COUNT: 1148

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

A process for making a high molecular weight poly(phosphoester) composition comprising:

- (i) a biologically active substance; and
- (ii) a poly(phosphoester) with the recurring monomeric units: ##STR1## wherein X is --O-- or --NR"--, where R" is H or alkyl; L is a divalent organic moiety, with the proviso that L cannot have the formula ##STR2## R' is H, alkyl, alkoxy, aryl, aryloxy, heterocyclic, or heterocycloxy; and n is from about 25 to 2000,

is described. The process comprises the steps of:

- (a) substantially dissolving p moles of a di--XH compound in a solvent comprising more than 75% toluene at a first temperature between about -75.degree. C. and +60 degree. C. to form a reaction mixture;
- (b) while maintaining the reaction mixture at the first temperature, adding q moles, where p.apprxeq.q, of a phosphorodihalo compound;
- (c) gradually increasing said first temperature at a rate of less than about 1.5.degree. C. per minute as necessary to achieve a second temperature between about 0.degree. C. and 150.degree. C., and mixing the reaction mixture at the second temperature to form the polymer of formula I; and
- (d) isolating the polymer of formula I.
- (e) incorporating the biologically active substance into the polymer of formula I.

# CAS INDEXING IS AVAILABLE FOR THIS PATENT.

DRWD . . . albuterol and dobutamine; (36) cardiovascular agents, such as aspirin (ASA) (enteric coated ASA); (37) .beta.-blocker antianginals, such as atenolol and \*\*\*propranolol\*\*\*; (38) calcium-channel blocker antianginals, such as nifedipine and verapamil; (39) nitrate antianginals, such as isosorbide dinitrate (ISDN); (40) cardiac glycoside. . . (41) class I antiarrhythmics, such as lidocaine, mexiletine, phenytoin, procainamide, and quinidine; (42) class II antiarrhythmics, such as atenolol, metoprolol, \*\*\*propranolol\*\*\* and timolol; (43) class III antiarrhythmics, such as amiodarone; (44) class IV antiarrhythmics, such as diltiazem and verapamil; (45) .alpha.-blocker. . . such as gemfibrozil and probucol; (53) bile acid sequestrant antilipemics, such as cholestyramine; (54) HMG-CoA reductase inhibitor antilipemics, such as \*\*\*lovastatin\*\*\* \*\*\*pravastatin\*\*\* ; (55) inotropes, such as amrinone, dobutamine, and

dopamine; (56) cardiac glycoside inotropes, such as digoxin; (57) thrombolytic agents, such as. . . naltrexone, and nicotine; (125) withdrawal substance abuse agents, such as bromocriptine; (126) minerals, such as iron, calcium, and magnesium; (127) \*\*\*vitamin\*\*\*

\*\*\*B\*\*\* compounds, such as cyanocobalamin ( \*\*\*vitamin\*\*\* \*\*\*B\*\*

.sub.12) and niacin ( \*\*\*vitamin\*\*\* \*\*\*B\*\*\* .sub.3); (128) vitamin

C compounds, such as ascorbic acid; and (129) vitamin D compounds, such as calcitriol.

L37 ANSWER 8 OF 16 USPATFULL

ACCESSION NUMBER: 1999:50718 USPATFULL

TITLE: Production of covered tablets

INVENTOR(S): Rosenberg, Joerg, Ellerstadt, Germany, Federal Republic

οf

Maier, Werner, Schifferstadt, Germany, Federal Republic

οf

Grabowski, Sven, Ludwigshafen, Germany, Federal

Republic of

Breitenbach, Jorg, Mannheim, Germany, Federal Republic

οf

PATENT ASSIGNEE(S): BASF Aktiengesellschaft, Ludwigshafen, Germany, Federal

Republic of (non-U.S. corporation)

19970620 PCT 371 date 19970620 PCT 102(e) date

NUMBER DATE

PRIORITY INFORMATION: DE 1994-4446468 19941223

DOCUMENT TYPE: Utility

PRIMARY EXAMINER: Dudash, Diana LEGAL REPRESENTATIVE: Keil & Weinkauf

NUMBER OF CLAIMS: 20 EXEMPLARY CLAIM: 1

NUMBER OF DRAWINGS: 1 Drawing Figure(s); 1 Drawing Page(s)

LINE COUNT: 506

AB The present invention is a process for the production of covered tablets by melt calendering in which the melt containing active ingredient is introduced between two sheets of the covering material into the molding rolls.

SUMM . . . isotretinoin, ketotifen, ketoconazole, ketoprofen, ketorolac, labetalol, lactulose, lecithin, levocarnitine, levodopa, levoglutamide, levonorgestrel, levothyroxine, lidocaine, lipase, lipoic acid, lisinopril, loperamide, lorazepam, \*\*\*lovastatin\*\*\*, medroxyprogesterone, menthol, methotrexate, methyldopa, methylprednisolone, metoclopramide, metoprolol, miconazole, midazolam, minocycline, minoxidil, misoprostol, morphine, multivitamin mixtures or combinations and mineral salts, . . . omeprazole, ondansetron, pancreatin, panthenol, pantothenic acid, paracetamol, penicillin G, penicillin V, phenoparbital, pentoxifylline, phenylephrine.

penicillin V, phenobarbital, pentoxifylline, phenylephrine,
phenylpropanolamine, phenytoin, piroxicam, polymyxin B, povidone-iodine,
 \*\*\*pravastatin\*\*\* , prednisolone, bromocriptine, propafenone,
 \*\*\*propranolol\*\*\* , pseudoephedrine, pyridoxine, quinidine, ramipril,

ranitidine, reserpine, retinol, riboflavin, rifampicin, rutoside, saccharin, salbutamol, salcatonin, salicylic acid, \*\*\*simvastatin\*\*\*, somatropin, sotalol, spironolactone, sucralfate, sulbactam, sulfamethoxazole, sulpiride, tamoxifen, tegafur, teprenone, terazosin, terbutaline, terfenadine, theophylline, thiamine, ticlopidine, timolol, tranexamic acid, tretinoin, triamcinolone acetonide, triamterene, trimethoprim, troxerutin, uracil, valproic acid, vancomycin, verapamil,

\*\*\*vitamins\*\*\* \*\*\*B\*\*\* .sub.1, B.sub.2, B.sub.4, B.sub.6, B.sub.12, D.sub.3, E, K, folinic acid, zidovudine.

L37 ANSWER 9 OF 16 USPATFULL

ACCESSION NUMBER: 1999:33594 USPATFULL

TITLE: Controlled release simvastatin delivery device INVENTOR(S): Rork, Gerald S., Lawrence, KS, United States

Pipkin, James D., Lawrence, KS, United States
PATENT ASSIGNEE(S): Merck & Co., Inc., Rahway, NJ, United States (U.S.

corporation)

US 1997-817129 19970801 (8)

WO 1995-US13693 19951019

19970801 PCT 371 date 19970801 PCT 102(e) date

RELATED APPLN. INFO.: Continuation of Ser. No. US 1994-327083, filed on 21

Oct 1994, now patented, Pat. No. US 5543154 which is a continuation-in-part of Ser. No. US 1993-118836, filed on 8 Sep 1993, now patented, Pat. No. US 5366738 which is a continuation of Ser. No. US 1992-902188, filed on 29 Jul 1992, now abandoned And a continuation-in-part of Ser. No. US 1991-815304, filed on 27 Dec 1991, now

abandoned

DOCUMENT TYPE:

Utility

PRIMARY EXAMINER:

NUMBER OF DRAWINGS:

Brouillette, D. Gabrielle

LEGAL REPRESENTATIVE:

Quagliato, Carol S.; Winokur, Melvin

NUMBER OF CLAIMS: 2 EXEMPLARY CLAIM: 1

7 Drawing Figure(s); 7 Drawing Page(s)

LINE COUNT: 1067

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

the number and size of the apertures in the coating.

AB Controlled delivery of a beneficial agent in a dispersion is provided using (i) a compressed core which contains the beneficial agent, a polymer which forms gelatinous microscopic particles upon hydration, and if desired, an agent to modulate the hydration; and (ii) a water insoluble coating which adheres to and surrounds the core and contains apertures which provide an area for the hydration and release of the dispersion. The release rate of the beneficial agent is a function of

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

DETD . . . as bephenium, hydroxynaphthoate, dichlorophen and dapsone; antineoplastics such as mechlorethamine, uracil mustard, 5-fluorouracil, 6-thioguanine and procarbazine; .beta.-blockers such as pindolol, \*\*\*propranolol\*\*\* , metoprolol, oxprenolol, timolol maleate, atenolol; hypoglycemic drugs such as insulin, isophane insulin; protamine zinc insulin suspension, globin zinc insulin, extended. . . tolazamide and chlorpropamide; antiulcer drugs such as cimetidine, ranitidine, famotidine and omeprazole; nutritional agents such as ascorbic acid, \*\*\*acid\*\*\* , choline, biotin, niacin, nicotinamide, \*\*\*folic\*\*\* pantothenic acid; essential amino acids; essential fats; ophthalmic drugs such as timolol maleate, pilocarpine nitrate, pilocarpine hydrochloride, atropine. . . on .alpha.-adrenergic receptors such as clonidine hydrochloride; analgesic drugs such as acetaminophen, oxycodone, hydrocodone, and propoxyphene; antihypercholesterolemic drugs \*\*\*simvastatin\*\*\* , \*\*\*pravastatin\*\*\* , \*\*\*lovastatin\*\*\* and genfibrozil; antiinfective drugs such as cefoxitin, cefazolin, cefotaxime, ciprofloxacin, cephalexin, norfloxacin, amprolium, ampicillin, amoxicillin, cefaclor, erythromycin, nitrofurantoin,

L37 ANSWER 10 OF 16 USPATFULL

ACCESSION NUMBER: 1998:143696 USPATFULL

minocycline, doxycycline,.

TITLE: Transdermal delivery of medications using a combination

of penetration enhancers

INVENTOR(S): Grasela, John C., 4521 Saluto Ct., San Diego, CA,

United States 92130

Grasela, Joseph E., 4767 Ocean Blvd., San Diego, CA,

United States 92109

Jubenville, Robert M., 550 Washington St., San Diego,

CA, United States 92103

McCloskey, Joseph J., 1167 Cooperwood, Bloomfield

Hills, MI, United States 48302

NUMBER DATE

```
PATENT INFORMATION:
                        US 5837289
                                         19981117
APPLICATION INFO.:
                        US 1996-685172 19960723 (8)
DOCUMENT TYPE:
                        Utility
PRIMARY EXAMINER:
                        Page, Thurman K.
ASSISTANT EXAMINER:
                        Shelborne, Kathryne E.
LEGAL REPRESENTATIVE:
                        Brown, Martin, Haller & McClain, LLP
NUMBER OF CLAIMS:
EXEMPLARY CLAIM:
NUMBER OF DRAWINGS:
                        1 Drawing Figure(s); 1 Drawing Page(s)
LINE COUNT:
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
      A composition and procedures for its formation and administration are
       described, which provide for a convenient, efficacious and simple
       transdermal administration of medications from a topically applied
      cream. No transmission through a membrane is involved. The composition
       incorporates at least two separate penetration enhancers which function
       synergistically to provide for rapid but controllable transport of the
      medication from the cream into the skin. The use of a plurality of
      penetration enhancers, at least one of which facilitates the separation
      of medication from the cream and at least a second of which alters the
      structure of the outer layers of skin, particularly the stratum corneum,
       enhances migration of the drug through the stratum corneum.
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
DETD
      . . . Vitamin E
      Vitamin B1
      Vitamin B2
      Vitamin B3
      Vitamin B6
      Vitamin B12
      Vitamin C
      Multivitamin Preparations
      Vitamin Combinations
      Antihyperlipidemic Agents
           ***Fluvastatin***
           ***Lovastatin***
           ***Pravastatin***
           ***Simvastatin***
      Probucol
      Niacin
      Dexothyroxine
      Clofibrate
      Gemfibrozil
      Cardiac Drugs
      Cardiac Glycosides
      Digitoxin
      Digoxin
      Antianginal Agents
      Nitroglycerin
      Isosorbide Dinitrate
      Isosorbide Mononitrate'
      Antiarrhythmic Agents

    Amphotericin B

      Griseofulvin
      Fluconazole
      Itraconazole
      Sulfonamides
      Sulfadiazine
      Sulfacytine
      Sulfamethoxazole
      Suflamethiazole
      Antimalarials
      Quinine Sulfate
      Mefloquine
      Quinacrine
      Doxycycline
      4-Aminoquinolone
      Compounds
      8-Aminoquinolone
      Compounds
                         ***Acid*** Antagonists
          ***Folic***
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Antituberculous Drugs
       Isoniazid
       Rifampin
       Rifabutin
       Ethambutol HCl
       Pyrazinamide
       Aminosalicylate Sodium
       Ethionamide
       Cycloserine
       Streptomycin Sulfate
       Capreomycin
       Amebicides
       Paromomycin
       Iodoquinol
       Metronidazole
         Octyl Salicylate
       Menthyl Anthranilate
       Digalloyl Trioleate
       Avobenzone
       Muscle Relaxants
       Carisoprodol
       Chlorphenesin
       Chlorzoxazone
       Cyclobenzaprine
       Metaxalone
       Methocarbamol
       Orphenadrine
       Diazepam
       Baclofen
       Antihypertensives
       Beta-Blockers
           ***Propranolol***
       Acebutolol
       Betaxolol
       Bisoprolol
       Esmolol
       Metoprolol
       Carteolol
       Nadolol
       Penbutolol
       Pindolol
       Sotalol
       Timolol
       Labetalol
       Ace Inhibitors
       Benazepril
       Captopril
       Enalapril
       Fosinopril
       Lisinopril
       Moexipril
L37 ANSWER 11 OF 16 USPATFULL
ACCESSION NUMBER:
                        1998:115859 USPATFULL
TITLE:
                        Method for inducing crystalline state transition in
                        medicinal substance
INVENTOR(S):
                        Nakamichi, Kouichi, Shiga, Japan
                        Izumi, Shougo, Kyoto, Japan
                        Oka, Masaaki, Osaka, Japan
PATENT ASSIGNEE(S):
                        Nippon Shinyaju Co., Ltd., Kyoto, Japan (non-U.S.
                        corporation)
                             NUMBER
                                           DATE
                        -----
PATENT INFORMATION:
                        US 5811547
                                         19980922
                        WO 9408561
                                         19940428
APPLICATION INFO .:
                        US 1995-416815
                                         19950609
                                                    (8)
                        WO 1993-JP1469
                                         19931013
                                         19950609
                                                   PCT 371 date
                                         19950609 PCT 102(e) date
RELATED APPLN. INFO.:
```

Continuation-in-part of Ser. No. US 1993-129133, filed

on 15 Nov 1993, now patented, Pat. No. US 5456923, issued on 10 Oct 1995

NUMBER DATE

PRIORITY INFORMATION: JP 1992-303085 19921014

DOCUMENT TYPE: Utility

PRIMARY EXAMINER: Shah, Mukund J.

ASSISTANT EXAMINER: Wong, K.

LEGAL REPRESENTATIVE: Graham & James LLP

NUMBER OF CLAIMS: 12

EXEMPLARY CLAIM: 1

NUMBER OF DRAWINGS: 10 Drawing Figure(s); 5 Drawing Page(s)

LINE COUNT: 1410

AB This invention has for its object to provide a method of inducing a transition in crystalline state of a crystallizable medicinal substance with great ease and improved efficiency and uniformity on a high production scale. According to the invention, an extruder is used for inducing a transition from one crystalline state (.DELTA.) to another crystalline state in a crystallizable medicinal substance.

# CLM What is claimed is:

. alprenolol hydrochloride, arotinolol hydrochloride, indenolol hydrochloride, oxprenolol hydrochloride, carteolol hydrochloride, pyrudicainide hydrochloride, bufetolol hydrochloride, bupranolol hydrochloride, procainamide hydrochloride, propafenone hydrochloride, \*\*\*propranolol\*\*\* hydrochloride, befunolol hydrochloride, verapamil hydrochloride, mexiletine hydrochloride, cibenzoline succinate, flecainide acetate, disopyramide, metoprolol tartrate, nadolol, pindolol, bisoprolol fumarate, timolol maleate,. . . nisoldipine, nitrendipine, nifedipine, hepronicate, bamethan sulfate, .tau.-oryzanol, clinofibrate, clofibrate, aluminium clofibrate, colestyramine, symvastatin, simfibrate, soysterol, dextran sulfate sodium, nicomol, niceritrol, \*\*\*pravastatin\*\*\* sodium, probucol, bezafibrate, polyenephos phatidylcholine, melinamide, ethyl linoleate, said cardiovascular drugs are selected from the group consisting of argatroban, alprostadil, . . . nitrate, thiamine disulfide, bisibuthiamine, bisbutytiamine, bisbentiamine, fursultiamine, prosultiamine, benfotiamine, pyridoxine hydrochloride, cobamamide, hydroxocobalamin acetate, cyanocobalamin, nicotinic acid, nicotinamide, pantethine, mecobalamin, \*\*\*folic\*\*\* \*\*\*acid\*\*\* , riboflavin butyrate, riboflavin, pyridoxamine phosphate, pyridoxal phosphate, riboflavin sodium phosphate, ascorbic acid, tocopherol calcium succinate, tocopherol acetate, phytonadione, menatetrenone, biotin,. .

L37 ANSWER 12 OF 16 USPATFULL

INVENTOR(S):

PATENT ASSIGNEE(S):

ACCESSION NUMBER: 96:113644 USPATFULL

TITLE: Controlled release drug suspension delivery device

Rork, Gerald S., Lawrence, KS, United States

Pipkin, James D., Lawrence, KS, United States

Merck& Co., Inc., Rahway, NJ, United States (U.S.

corporation)

NUMBER DATE

PATENT INFORMATION: US 5582838 19961210 APPLICATION INFO.: US 1994-363451 19941222 (8)

DOCUMENT TYPE: Utility

PRIMARY EXAMINER: Spear, James M.

LEGAL REPRESENTATIVE: Bigley, Francis P.; Daniel, Mark R.

NUMBER OF CLAIMS: 23 EXEMPLARY CLAIM: 1

NUMBER OF DRAWINGS: 6 Drawing Figure(s); 4 Drawing Page(s)

LINE COUNT: 876

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

AB A device is disclosed for the controlled delivery of a beneficial agent, the device consisting of (i) a core comprising at least two layers, wherein at least one layer comprises a beneficial agent and a polymer which forms microscopic gel beads upon hydration and at least one layer which comprises a polymer which forms microscopic gel beads upon hydration; and (ii) an impermeable, insoluble coating which adheres to

and surrounds the core and contains apertures which provide an area for the hydration and release of the microscopic gel beads.

### CAS INDEXING IS AVAILABLE FOR THIS PATENT.

. . . as bephenium, hydroxynaphthoate, dichlorophen and dapsone; DETD antineoplastics such as mechlorethamine, uracil mustard, 5-fluorouracil, 6-thioguanine and procarbazine; .beta.-blockers such as pindolol, \*\*\*propranolol\*\*\* , metoprolol, oxprenolol, timolol maleate, atenolol; hypoglycemic drugs such as insulin, isophane insulin; protamine zinc insulin suspension, globin zinc insulin, extended. . . tolazamide and chlorpropamide; antiulcer drugs such as cimetidine, ranitidine, famotidine and omeprazole nutritional agents such as ascorbic acid, niacin, nicotinamide, \*\*\*folic\*\*\* \*\*\*acid\*\*\* , choline, biotin, pantothenic acid; essential amino acids; essential fats; ophthalmic drugs such as timolol maleate, pilocarpine nitrate, pilocarpine hydrochloride, atropine. . . on .alpha.-adrenergic receptors such as clonidine hydrochloride; alnalgesic drugs such as acetaminophen, oxycodone, hydrocodone, and propoxyphene; antihypercholesterolemic drugs such as \*\*\*simvastatin\*\*\* , \*\*\*pravastatin\*\*\* , \*\*\*lovastatin\*\*\* and genfibrozil; antiinfective drugs such as cefoxitin, cefazolin, cefotaxime, ciprofloxacin, cephalexin, norfloxacin, amprolium, ampicillin, amoxicillin, cefacloi, erythromycin, nitrofurantoin, minocycline, doxycycline, . . .

L37 ANSWER 13 OF 16 USPATFULL

ACCESSION NUMBER: 96:70200 USPATFULL

TITLE: Controlled release nifedipine delivery device INVENTOR(S): Rork, Gerald S., Lawrence, KS, United States Pipkin, James D., Lawrence, KS, United States

PATENT ASSIGNEE(S): Merck & Co., Inc., Rahway, NJ, United States (U.S.

corporation)

NUMBER DATE

PATENT INFORMATION: US 5543154 19960806 APPLICATION INFO.: US 1994-327083 19941021 (8)

RELATED APPLN. INFO.: Continuation-in-part of Ser. No. US 1993-118836, filed

on 8 Sep 1993, now patented, Pat. No. US 5366738 which is a continuation of Ser. No. US 1992-902188, filed on

29 Jul 1992, now abandoned which is a

continuation-in-part of Ser. No. US 1991-815304, filed

on 27 Dec 1991, now abandoned

DOCUMENT TYPE: Utility

PRIMARY EXAMINER: Phelan, D. Gabrielle

LEGAL REPRESENTATIVE: Bigley, Francis P.; Daniel, Mark R.

NUMBER OF CLAIMS: 16 EXEMPLARY CLAIM: 1

NUMBER OF DRAWINGS: 7 Drawing Figure(s); 7 Drawing Page(s)

LINE COUNT: 933

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

AB A device for the controlled delivery of a beneficial agent as a gelatinous dispersion consisting of (i) a core which contains a beneficial agent, a polymer which forms gelatinous micoroscopic particles upon hydration and if desired an agent to modulate the hydration of the polymer; and (ii) an impermeable, insoluble coating which adheres to and surrounds the core and contains apertures which provide an area for the hydration and release of a disperson comprising gelatinous microscopic particles.

### CAS INDEXING IS AVAILABLE FOR THIS PATENT.

DETD . . . as bephenium, hydroxynaphthoate, dichlorophen and dapsone; antineoplastics such as mechlorethamine, uracil mustard, 5-fluorouracil, 6-thioguanine and procarbazine; .beta.-blockers such as pindolol, \*\*\*propranolol\*\*\* , metoprolol, oxprenolol, timolol maleate, atenolol; hypoglycemic drugs such as insulin, isophane insulin, protamine zinc insulin suspension, globin zinc insulin, extended. . . tolazamide and chlorpropamide; antiulcer drugs such as cimetidine, ranitidine, famotidine and omeprazole; nutritional agents such as ascorbic acid, niacin, nicotinamide, \*\*\*folic\*\*\* \*\*\*acid\*\*\* , choline, biotin, pantothenic acid; essential amino acids; essential fats; ophthalmic drugs such as timolol maleate, pilocarpine nitrate, pilocarpine hydrochloride, attopine. . . on .alpha.-adrenergic receptors such as

clonidine hydrochloride; analgesic drugs such as acetaminophen, oxycodone, hydrocodone, and propoxyphene; antihypercholesterolemic drugs such as \*\*\*simvastatin\*\*\* , \*\*\*pravastatin\*\*\* , \*\*\*lovastatin\*\*\* and gemfibrozil; antiinfective drugs such as cefoxitin, cefazolin, cefotaxime, ciprofloxacin, cephalexin, norfloxacin, amprolium, ampicillin, amoxicillin, cefaclor, erythromycin, nitrofurantoin, minocycline, doxycycline, . . .

L37 ANSWER 14 OF 16 USPATFULL

ACCESSION NUMBER: 94:102004 USPATFULL

TITLE: Controlled release drug dispersion delivery device

INVENTOR(S): Rork, Gerald S., Lawrence, KS, United States
Pipkin, James D., Lawrence, KS, United States

PATENT ASSIGNEE(S): Merck & Co., Inc., Rahway, NJ, United States (U.S.

corporation)

NUMBER DATE

PATENT INFORMATION: US 5366738 19941122 APPLICATION INFO.: US 1993-118836 19930908 (8)

RELATED APPLN. INFO.: Continuation of Ser. No. US 1982-902188, filed on 29

Jul 1982, now abandoned which is a continuation-in-part of Ser. No. US 1991-815304, filed on 27 Dec 1991, now

abandoned

DOCUMENT TYPE: Utility

PRIMARY EXAMINER: Phelan, D. Gabrielle

LEGAL REPRESENTATIVE: Bigley, Francis P.; Daniel, Mark R.; DiPrima, Joseph F.

NUMBER OF CLAIMS: 18 EXEMPLARY CLAIM: 1

NUMBER OF DRAWINGS: 7 Drawing Figure(s); 7 Drawing Page(s)

LINE COUNT: 887

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

AB A device for the controlled delivery of a beneficial agent as a gelatinous dispersion consisting of (i) a core which contains a beneficial agent, a polymer which forms gelatinous microscopic particles upon hydration and if desired an agent to modulate the hydration of the polymer; and (ii) an impermeable, insoluble coating which adheres to and surrounds the core and contains apertures which provide an area for the hydration and release of a dispersion comprising gelatinous microscopic particles.

### CAS INDEXING IS AVAILABLE FOR THIS PATENT.

DETD . . . as bephenium, hydroxynaphthoate, dichlorophen and dapsone; antineoplastics such as mechlorethamine, uracil mustard, 5-fluorouracil, 6-thioguanine and procarbazine; .beta.-blockers such as pindolol, \*\*\*propranolol\*\*\* , metoprolol, oxprenolol, timolol maleate, atenolol; hypoglycemic drugs such as insulin, isophane insulin, protamine zinc insulin suspension, globin zinc insulin, extended. . . tolazamide and chlorpropamide; antiulcer drugs such as cimetidine, ranitidine, famotidine and omeprazole; nutritional agents such as ascorbic acid, niacin, nicotinamide, \*\*\*folic\*\*\* \*\*\*acid\*\*\* , choline, biotin, pantothenic acid; essential amino acids; essential fats; ophthalmic drugs such as timolol maleate, pilocarpine nitrate, pilocarpine hydrochloride, atropine. . . on .alpha.-adrenergic receptors such as clonidine hydrochloride; analgesic drugs such as acetaminophen, oxycodone, hydrocodone, and propoxyphene; antihypercholesterolemic drugs such as \*\*\*simvastatin\*\*\* , \*\*\*pravastatin\*\*\* , \*\*\*lovastatin\*\*\* and gemfibrozil; antiinfective drugs such as cefoxitin, cefazolin, cefotaxime, ciprofloxacin, cephalexin, norfloxacin, amprolium, ampicillin, amoxicillin, cefaclor, erythromycin, nitrofurantoin, minocycline, doxycycline, . . .

L37 ANSWER 15 OF 16 USPATFULL

ACCESSION NUMBER: 94:84091 USPATFULL

TITLE: Spheronization process using charged resins

INVENTOR(S): McClelland, Gregory A., Lawrence, KS, United States

Zentner, Gaylen M., Lawrence, KS, United States

PATENT ASSIGNEE(S): Merck & Co., Inc., Rahway, NJ, United States (U.S. corporation)

•

NUMBER DATE

PATENT INFORMATION: US 5350584 19940927 APPLICATION INFO.: US 1992-906226 19920626 (7)

DOCUMENT TYPE: Utility

PRIMARY EXAMINER: Page, Thurman K.
ASSISTANT EXAMINER: Kulkosky, Peter F.

LEGAL REPRESENTATIVE: Bigley, Francis P.; Daniel, Mark R.; DiPrima, Joseph F.

NUMBER OF CLAIMS: 13 EXEMPLARY CLAIM: 1 LINE COUNT: 468

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

The invention comprises a novel process for the spheronization of charged resins. Spherical multiparticlates are produced which range in size from 0.3 mm to 3 mm in diameter. The spherical particle product is microcrystalline-free. The process consists of the steps of mixing followed by wet granulation, spheronization and drying.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

DETD . . . as bephenium, hydroxynaphthoate, dichlorophen and dapsone; antineoplastics such as mechlorethamine, uracil mustard, 5-fluorouracil, 6-thioguanine and procarbazine; .beta.-blockers such as pindolol, \*\*\*propranolol\*\*\* , metoprolol, oxprenolol, timolol maleate, atenolol; hypoglycemic drugs such as insulin, isophane insulin, protamine zinc insulin suspension, globin zinc insulin, extended. . . tolazamide and chlorpropamide; antiulcer drugs such as cimetidine, ranitidine, famotidine and omeprazole; nutritional agents such as ascorbic acid, niacin, nicotinamide, \*\*\*folic\*\*\* \*\*\*acid\*\*\* , choline, biotin, pantothenic acid; essential amino acids; essential fats; ophthalmic drugs such as timolol maleate, pilocarpine nitrate, pilocarpine hydrochloride, atropine. . . on .alpha.-adrenergic receptors such as clonidine hydrochloride; analgesic drugs such as acetaminophen, oxycodone, hydrocodone, and propoxyphene; antihypercholesterolemic drugs \*\*\*simvastatin\*\*\* , \*\*\*pravastatin\*\*\* , \*\*\*lovastatin\*\*\* and gemfibrozil; antiinfective drugs such as cefoxitin, cefazolin, cefotaxime, ciprofloxacin, cephalexin, norfloxacin, amprolium, ampicillin, amoxicillin, cefaclor, erythromycin, nitrofurantoin, minocycline, doxycycline,.

L37 ANSWER 16 OF 16 USPATFULL

ACCESSION NUMBER: 93:89448 USPATFULL

TITLE: Process for producing a tablet core aperture INVENTOR(S): Appel; Leah E., Lawrence, KS, United States

Zentner, Gaylen M., Lawrence, KS, United States
PATENT ASSIGNEE(S): Merck & Co., Inc., Rahway, NJ, United States (U.S.

corporation)

NUMBER DATE

PATENT INFORMATION: US 5256440 19931026 APPLICATION INFO.: US 1992-902187 19920622 (7)

DOCUMENT TYPE: Utility

PRIMARY EXAMINER: Owens, Terry J. ASSISTANT EXAMINER: Cameron, Erma

LEGAL REPRESENTATIVE: Bigley, Francis P.; DiPrima, Joseph F.

NUMBER OF CLAIMS: 17 EXEMPLARY CLAIM: 1

NUMBER OF DRAWINGS: 3 Drawing Figure(s); 3 Drawing Page(s)

LINE COUNT: 502

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

AB Process for preparing and film coating a dosage form. An intagliated dosage form core is produced by inscribing one or more areas on the surface of the dosage form core prior to coating. An aqueous dispersion of a polymeric coating is then applied to the intagliated dosage form core. When placed in an environment of use, the film coating within the circumscribed region of the dosage form surface is reproducibly expelled, leaving a coated core tablet with a predefined aperture in the coating which exposes a discrete portion of the core surface to the environment of use.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

DETD . . . as bephenium, hydroxynaphthoate, dichlorophen and dapsone; antineoplastics such as mechlorethamine, uracil mustard, 5-fluorouracil, 6-thioguanine and procarbazine; .beta.-blockers such as pindolol,

brobrancio , metoprolol, oxprenolol, timolol maleate, atenolol; hypoglycemic drugs such as insulin, isophane insulin, protamine zinc insulin suspension, globin zinc insulin, extended. . . tolazamide and chlorpropamide; antiulcer drugs such as cimetidine, ranitidine, famotidine and omeprazole; nutritional agents such as ascorbic acid, niacin, nicotinamide, \*\*\*folic\*\*\* \*\*\*acid\*\*\* , choline, biotin, pantothenic acid; essential amino acids; essential fats; ophthalmic drugs such as timolol maleate, pilocarpine nitrate, pilocarpine hydrochloride, atropine. . . on .alpha.-adrenergic receptors such as clonidine hydrochloride; analgesic drugs such as acetaminophen, oxycodone, hydrocodone, and propoxyphene; antihypercholesterolemic drugs \*\*\*simvastatin\*\*\* , \*\*\*pravastatin\*\*\* , \*\*\*lovastatin\*\*\* and gemfibrozil; antiinfective drugs such as cefoxitin, cefazolin, cefotaxime, ciprofloxacin, cephalexin, norfloxacin, amprolium, ampicillin, amoxicillin, cefaclor, erythromycin, nitrofurantoin, minocycline, doxycycline,. . .

=> FIL STNGUIDE COST IN U.S. DOLLARS

SINCE FILE TOTAL ENTRY SESSION 193.04 261.33

FULL ESTIMATED COST

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FILE CONTAINS CURRENT INFORMATION.
LAST RELOADED: May 18, 2001 (20010518/UP).

=> SAVE L1,L3,L8,L9,L11,L12,L13,L14,L15,L16 SAN09717987/L L# LIST L1,L3,L8,L9,L11,L12,L13,L14,L15,L16 HAS BEEN SAVED AS 'SAN09717987/L'

=> FIL MEDLINE CAPLUS EMBASE BIOSIS USPATFULL COST IN U.S. DOLLARS

FULL ESTIMATED COST SINCE FILE TOTAL ENTRY SESSION 0.00 261.33

FILE 'MEDLINE' ENTERED AT 13:14:48 ON 23 MAY 2001

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=> fil stng COST IN U.S. DOLLARS

SINCE FILE TOTAL ENTRY SESSION 3.43 264.76

FULL ESTIMATED COST

FILE 'STNGUIDE' ENTERED AT 13:14:59 ON 23 MAY 2001
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FILE CONTAINS CURRENT INFORMATION. LAST RELOADED: May 18, 2001 (20010518/UP).

=> d his

```
1 S ATENOLOL/CN
T.1
L2
              0 S PROPANOLOL/CN
             1 S TIMOLOL/CN
L3
              0 S METAPROLOL/CN
L4
L5
              2 $ INDERAL
L6
              0 S METAPROLOL
L7
              0 S METAPROLOLOL
L8
             1 S METOPROLOL/CN
             1 S PROPRANOLOL/CN
L9
L10
             1 S TIMOLOL/CN
             1 S ATORVASTATIN/CN
L11
             1 S CERIVASTATIN/CN
L12
L13
             1 S PRAVASTATIN/CN
L14
             1 S FLUVASTATIN/CN
L15
             1 S LOVASTATIN/CN
L16
             1 S SIMVASTATIN)CN
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     23 MAY 2001
         216829 S L11-16 OR ATORVASTATIN OR CERIVASTATIN OR PRAVASTATIN OR FLUV
L17
         202196 S L1 OR L8-10 OR ATENOLOL OR TIMOLOL OR PROPRANOLOL OR METOPROL
L18
L19
           1018 S L17 (S) L18
             28 S L17 (W) L18
L20
             28 S L20 2001
L21
             28 S L20 2000
L22
L23
          23940 S L11-16 OR ATORVASTATIN OR CERIVASTATIN OR PRAVASTATIN OR FLUV
L24
             72 S L23 (S) (L1 OR ATENOLOL)
              2 S L23 (W) (L1 OR ATENOLOL)
L25
L26
             46 S L23 (S) (L3 OR TIMOLOL)
L27
             0 S L23 (A) (L3 OR TIMOLOL)
L28
             46 S L23 (P) (L3 OR TIMOLOL)
            44 DUP REM L28 (2 DUPLICATES REMOVED)
L29
L30
             23 S L29 (S) FOLIC ACID
            58 S L23 (S) (L8 OR METOPROLOL)
L31
            48 DUP REM L31 (10 DUPLICATES REMOVED)
L32
             39 S L32 (S) (FOLIC ACID OR FOLATE OR VITAMIN E)
L33
             17 S L32 (S) (FOLIC ACID OR FOLATE OR VITAMIN B)
L34
L35
             64 S L23 (S) (L9 OR PROPRANOLOL)
L36
             16 S L35 (S) (FOLIC ACID OR FOLATE OR VITAMIN B)
L37
             16 DUP REM L36 (0 DUPLICATES REMOVED)
     FILE 'STNGUIDE' ENTERED AT 13:12:54 ON 23 MAY 2001
                SAVE L1, L3, L8, L9, L11, L12, L13, L14, L15, L16 SAN09717987/L
     FILE 'MEDLINE, CAPLUS, EMBASE, BIOSIS, USPATFULL' ENTERED AT 13:14:48 ON
     23 MAY 2001
     FILE 'STNGUIDE' ENTERED AT 13:14:59 ON 23 MAY 2001
=> SAVE L17-137 SAN09717987b/L
L# LIST L17-L37 HAS BEEN SAVED AS 'SAN09717987B/L'
=> log h
                                                  SINCE FILE
COST IN U.S. DOLLARS
                                                                  TOTAL
                                                       ENTRY
                                                                SESSION
                                                        0.00
                                                                 264.76
FULL ESTIMATED COST
 SESSION WILL BE HELD FOR 60 MINUTES
STN INTERNATIONAL SESSION SUSPENDED AT 13:17:06 ON 23 MAY 2001
Connection closed by remote host
Trying 3106016892...Open
Welcome to STN International! Enter x:x
LOGINID:ssspta1617srh
PASSWORD:
 * * * * * RECONNECTED TO STN INTERNATIONAL * * * * * *
SESSION RESUMED IN FILE 'REGISTRY' AT 13:57:25 ON 25 MAY 2001
FILE 'REGISTRY' ENTERED AT 13:57:25 ON 25 MAY 2001
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```

FILE 'REGISTRY' ENTERED AT 12:39:09 ON 23 MAY 2001

COST IN U.S. DOLLARS

FULL ESTIMATED COST

=> fil medline
COST IN U.S. DOLLARS

FULL ESTIMATED COST

SINCE FILE
TOTAL
ENTRY
SESSION
ENTRY
SESSION
140.29
142.97

FILE 'MEDLINE' ENTERED AT 13:57:31 ON 25 MAY 2001

FILE LAST UPDATED: 21 MAY 2001 (20010521/UP). FILE COVERS 1958 TO DATE.

On April 22, 2001, MEDLINE was reloaded. See HELP RLOAD for details.

MEDLINE now contains new records from the former NLM HEALTH STAR database. These records have an Entry Date and Update Date of 20010223.

MEDLINE thesauri in the /CN, /CT, and /MN fields incorporate the MeSH 2001 vocabulary. Enter HELP THESAURUS for details.

The OLDMEDLINE file segment now contains data from 1958 through 1965. Enter HELP CONTENT for details.

Left, right, and simultaneous left and right truncation are available in the Basic Index. See HELP SFIELDS for details.

THIS FILE CONTAINS CAS REGISTRY NUMBERS FOR EASY AND ACCURATE SUBSTANCE IDENTIFICATION.

```
=> e beta blockers
                            BET5P/BI
E1
               4
             392102 BETA/BI
E2
                  0 --> BETA BLOCKERS/BI
E3
           0 --> BETA BLOCKERS/BI
56 BETA0/BI
1 BETA0HEMOLYTIC/BI
6646 BETA1/BI
17 BETA10/BI
1 BETA100/BI
1 BETA101/BI
2 BETA102/BI
3 BETA104/BI
2 BETA106/BI
E4
E5
E6
E7
E8
E9
E10
E11
E12
```

E#	FREQUENCY	AT	TERM
E13	0	2	BETA ASPARTIC ACID/CT
E14	0	2	BETA ATRIAL NATRIURETIC PEPTIDE/CT
E15	0	>	BETA BLOCKERS/CT
E16	0	2	BETA BLOCKERS, ADRENERGIC/CT
E17	0	2	BETA BUNGAROTOXIN/CT
E18	0	2	BETA CARBOLINES/CT
E19	2771	24	BETA CAROTENE/CT
E20	208		BETA CAROTENE: AA, ANALOGS & DERIVATIVES/CT
E21	294		BETA CAROTENE: AD, ADMINISTRATION & DOSAGE/CT
E22	47		BETA CAROTENE: AE, ADVERSE EFFECTS/CT
E23	2		BETA CAROTENE: AI, ANTAGONISTS & INHIBITORS/CT
E24	109		BETA CAROTENE: AN, ANALYSIS/CT

=> e e16+all
E25 0 --> beta Blockers, Adrenergic/CT
E26 21982 USE Adrenergic beta-Antagonists/CT
\*\*\*\*\*\*\*\*\* END \*\*\*\*\*\*\*\*

# => e e26

ADDITIONAL TERMS AVAILABLE BY USING "ADRENERGIC BETA-ANTAGONISTS+XUSE/CT" E# FREQUENCY AT TERM.

			'				
E27	2460		ADRENERGIC	BETA-AGONISTS:	TU,	THERAPEUTIC USE	CT/
E28	71		ADRENERGIC	BETA-AGONISTS:	UR,	URINE/CT	
E29	21982	57>	ADRENERGIC	BETA-ANTAGONIS	rs/c	Γ	

```
E30
          1975
                         ADRENERGIC BETA-ANTAGONISTS: AD, ADMINISTRATION & DOSA
                         GE/CT
          2180
                         ADRENERGIC BETA-ANTAGONISTS: AE, ADVERSE EFFECTS/CT
E31
                         ADRENERGIC BETA-ANTAGONISTS: AI, ANTAGONISTS & INHIBIT
E32
            47
                         ORS/CT
                         ADRENERGIC BETA-ANTAGONISTS: AN, ANALYSIS/CT
E33
           146
E34
           398
                         ADRENERGIC BETA-ANTAGONISTS: BL, BLOOD/CT
E35
             8
                         ADRENERGIC BETA-ANTAGONISTS: CF, CEREBROSPINAL FLUID/C
E36
           190
                         ADRENERGIC BETA-ANTAGONISTS: CH, CHEMISTRY/CT
E37
            57
                         ADRENERGIC BETA-ANTAGONISTS: CL, CLASSIFICATION/CT
                         ADRENERGIC BETA-ANTAGONISTS: CS, CHEMICAL SYNTHESIS/CT
E38
           245
=> e e29+all
E39
                 BT6
                       D Chemicals and Drugs/CT
                        Chemical Actions and Uses/CT
E40
             0
                  BT5
E41
             0
                   BT4
                         Chemical Actions/CT
E42
             0
                  BT5
                        D Chemicals and Drugs/CT
E43
             0
                   BT4
                         Neurotransmitters and Neurotransmitter Agents/CT
E44
            40
                    BT3
                          Neurotransmitter Agents/CT
           544
E45
                     BT2
                           Adrenergic Agents/CT
E46
           307
                      BT1
                             Adrenergic Antagonists/CT
E47
         21982
                              Adrenergic beta-Antagonists/CT
E48
         21982
                       MN
                              D14.100.50.200.200./CT
E49
         21982
                       MN
                              D27.505.583.50.200.200./CT
                        DC
                               an INDEX MEDICUS major descriptor
                        NOTE Drugs that bind to but do not activate
                               beta-adrenergic receptors thereby blocking the
                               actions of beta-adrenergic agonists. Adrenergic
                               beta-antagonists are used for treatment of
                               hypertension, cardiac arrythmias, angina
                               pectoris, glaucoma, migraine headaches, and
                               anxiety.
                         INDX
                               GEN or unspecified; prefer specifics; do not
                               confuse with ADRENERGIC BETA-AGONISTS; DF: ADREN
                               BETA ANTAG
                              AD AE AN BL CF CH CL CS CT DU EC HI IM IP ME PD
                         AQ
                              PK PO RE SD ST TO TU UR
                         PNTE
                               Sympatholytics (1966-1968)
                         HNTE
                               95: was ADRENERGIC BETA RECEPTOR BLOCKADERS
                               1969-94 (Prov 1969-72)
                         ONTE
                               use ADRENERGIC BETA-ANTAGONISTS to search
                               ADRENERGIC BETA RECEPTOR BLOCKADERS 1973-94 (as
                               Prov 1969-72)
                        MHTH
                               NLM (1969)
E50
             0
                        UF
                               ADREN BETA ANTAG/CT
E51
                        UF
                               Adrenergic beta Antagonists/CT
E52
                         UF
                               Adrenergic beta Receptor Blockaders/CT
E53
             0
                        UF
                               Adrenergic beta-Blockers/CT
E54
             0
                        UF
                               Adrenergic beta-Receptor Blockaders/CT
E55
             0
                        UF
                               Agents, beta-Adrenergic Blocking/CT
E56
             0
                        UF
                               Blockaders, Adrenergic beta-Receptor/CT
E57
             0
                        UF
                               Blockaders, beta-Adrenergic Receptor/CT
E58
             0
                        UF
                               Blockers, beta-Adrenergic/CT
E59
             0
                        UF
                               Blocking Agents, beta-Adrenergic/CT
E60
             0
                        UF
                               Receptor Blockaders, beta-Adrenergic/CT
E61
             0
                        UF
                               beta Adrenergic Blockers/CT
E62
             0
                        UF
                              tbeta Adrenergic Blocking Agents/CT
E63
             0
                        UF
                               beta Adrenergic Receptor Blockaders/CT
             0
E64
                        UF
                               beta Blockers, Adrenergic/CT
E65
             0
                        UF
                               beta-Adrenergic Blockers/CT
             0
E66
                        UF
                               beta-Adrenergic Blocking Agents/CT
E67
             0
                         UF
                               beta-Adrenergic Receptor Blockaders/CT
E68
             0
                         UF
                               beta-Antagonists, Adrenergic/CT
E69
             0
                         UF
                               beta-Blockers, Adrenergic/CT
E70
             0
                        UF
                               beta-Receptor Blockaders, Adrenergic/CT
E71
           751
                        NT1
                               Acebutolo1/CT
E72
           988
                        NT1
                               Alprenolol/CT
E73
                         NT2
          1197
                                Dihydroalprenolol/CT
E74
          3275
                         NT1
                               Atenolol/CT
E75
           440
                        NT1
                               Betaxolol/CT
           347
                        NT1
E76
                               Bisoprolol/CT
```

```
E78
           160
                        NT1
                              Butoxamine/CT
E79
           246
                        NT1
                              Carteolol/CT
E80
           319
                        NT1
                              Celiprolol/CT
E81
          1197
                        NT1
                              Dihydroalprenolol/CT
E82
          684
                        NT1
                            . Iodocyanopindolol/CT
E83
          1436
                        NT1
                            Labetalol/CT
E84
          193
                              Levobunolol/CT
                        NT1
E85
          240
                        NT1
                              Metipranolol/CT
E86
          3094
                        NT1
                              Metoprolol/CT
E87
          595
                       NT1
                              Nadolol/CT
E88
          977
                       NT1
                              Oxprenolol/CT
E89
          171
                       NT1
                              Penbutolol/CT
E90
          3378
                       NT1
                              Pindolol/CT
E91
          684
                        NT2
                              Iodocyanopindolol/CT
E92
          1485
                        NT1
                              Practolol/CT
E93
         27116
                        NT1
                              Propranolol/CT
E94
          1432
                        NT1
                              Sotalol/CT
E95
          2188
                        NT1
                              Timolol/CT
****** END ******
=> index bioscience
FILE 'DRUGMONOG' ACCESS NOT AUTHORIZED
COST IN U.S. DOLLARS
                                                  SINCE FILE
                                                                  TOTAL
                                                       ENTRY
                                                                SESSION
FULL ESTIMATED COST
                                                        0.90
                                                                 143.87
INDEX 'ADISALERTS, ADISINSIGHŤ, AGRICOLA, ANABSTR, AQUASCI, BIOBUSINESS,
       BIOCOMMERCE, BIOSIS, BIOTECHABS, BIOTECHDS, BIOTECHNO, CABA, CANCERLIT,
       CAPLUS, CEABA-VTB, CEN, CIN, CONFSCI, CROPB, CROPU, DDFB, DDFU, DGENE,
       DRUGB, DRUGLAUNCH, DRUGMONOG2, DRUGNL, ... 'ENTERED AT 13:59:25 ON 25 MAY 2001
59 FILES IN THE FILE LIST IN STNINDEX
Enter SET DETAIL ON to see search term postings or to view
search error messages that display as 0* with SET DETAIL OFF.
=> s Adrenergic beta (w) (Antagonists or block? or inhib?)
              FILE ADISALERTS
          3
              FILE AGRICOLA
          1
              FILE ANABSTR
<----> User Break---->
=> s beta (w) (Antagonists or block? or inhib?)
       7690
              FILE ADISALERTS
              FILE ADISINSIGHT
        145
        115
              FILE AGRICOLA
        297
              FILE ANABSTR
         29
              FILE AQUASCI
        430
              FILE BIOBUSINESS
         17
              FILE BIOCOMMERCE
      17145
              FILE BIOSIS
              FILE BIOTECHABS
         74
         74
              FILE BIOTECHDS
              FILE BIOTECHNO
       1022
              FILE CABA
        414
  12 FILES SEARCHED...
      1596
              FILE CANCERLIT
      10155
              FILE CAPLUS
         25
              FILE CEABA-VTB
         17
              FILE CEN
        294
              FILE CIN
              FILE CONFSCI
        535
              FILE CROPB
         3
         22
              FILE CROPU
 20 FILES SEARCHED...
      1012
              FILE DDFB
      10125
              FILE DDFU
        416
              FILE DGENE
       1012
              FILE DRUGB
       2180
              FILE DRUGLAUNCH
```

E77

159

146

FILE DRUGNL

NT1

Bupranolol/CT

```
13971
              FILE DRUGU
         96
              FILE DRUGUPDATES
        170
              FILE EMBAL
      18564
              FILE EMBASE
  31 FILES SEARCHED...
       2054
              FILE ESBIOBASE
         41
              FILE FROSTI
         26
              FILE FSTA
         28
              FILE GENBANK
         64
              FILE HEALSAFE
              FILE IFIPAT
        285
       1970
              FILE JICST-EPLUS
          2
              FILE KOSMET
       1139
              FILE LIFESCI
  42 FILES SEARCHED...
              FILE MEDICONF
         15
      31566
              FILE MEDLINE
         65
              FILE NIOSHTIC
         57
              FILE NTIS
              FILE OCEAN
          6
      12494
              FILE PASCAL
        197
              FILE PHAR
              FILE PHIC
         4
       2290
              FILE PHIN
       2494
              FILE PROMT
  52 FILES SEARCHED...
      12590
              FILE SCISEARCH
              FILE SYNTHLINE
       9451
              FILE TOXLINE
       6577
              FILE TOXLIT
       2778
              FILE USPATFULL
       1134
              FILE WPIDS
  58 FILES SEARCHED...
       1134
              FILE WPINDEX
  56 FILES HAVE ONE OR MORE ANSWERS,
                                       59 FILES SEARCHED IN STNINDEX
L10 QUE BETA (W) (ANTAGONISTS OR BLOCK? OR INHIB?)
=> s cholester? (W) (lower? or reduc? or decres?)
        893
              FILE ADISALERTS
         93
              FILE ADISINSIGHT
        423
              FILE AGRICOLA
         11
              FILE ANABSTR
         11
              FILE AQUASCI
        638
              FILE BIOBUSINESS
         34
              FILE BIOCOMMERCE
   7 FILES SEARCHED...
       2937
              FILE BIOSIS
         44
              FILE BIOTECHABS
         44
              FILE BIOTECHDS
        182
              FILE BIOTECHNO
        758
              FILE CABA
        148
              FILE CANCERLIT
       2595
              FILE CAPLUS
         31
              FILE CEABA-VTB
         48
              FILE CEN
        369
              FILE CIN
         84
              FILE CONFSCI
  18 FILES SEARCHED...
         2
              FILE CROPU
         64
              FILE DDFB
              FILE DDFU
        777
        338
              FILE DGENE
         64
              FILE DRUGB
         31
              FILE DRUGLAUNCH
         42
              FILE DRUGNL
       1013
              FILE DRUGU
         30
              FILE DRUGUPDATES
         42
              FILE EMBAL
       2724
              FILE EMBASE
        732
              FILE ESBIOBASE
```

```
FILE FOMAD
         65
              FILE FOREGE
        877
              FILE FROSTI
        365
              FILE FSTA
         1
              FILE GENBANK
          7
              FILE HEALSAFE .
              FILE IFIPAT
        299
        220
              FILE JICST-EPLUS
              FILE KOSMET
        1
        104
              FILE LIFESCI
         8
              FILE MEDICONF
       2622
              FILE MEDLINE
        15
              FILE NIOSHTIC
         25
              FILE NTIS
  46 FILES SEARCHED...
          2
              FILE OCEAN
       1080
              FILE PASCAL
         55
              FILE PHAR
              FILE PHIC
        488
              FILE PHIN
       3542
              FILE PROMT
       2659
              FILE SCISEARCH
              FILE SYNTHLINE
              FILE TOXLINE
        605
  55 FILES SEARCHED...
        813
              FILE TOXLIT
       1394
              FILE USPATFULL
        853
              FILE WPIDS
  58 FILES SEARCHED...
              FILE WPINDEX
        853
  57 FILES HAVE ONE OR MORE ANSWERS,
                                        59 FILES SEARCHED IN STNINDEX
    QUE CHOLESTER? (W) (LOWER? OR REDUC? OR DECRES?)
=> s 110 (s) 111
         10
             FILE ADISALERTS
         1
              FILE AGRICOLA
         19 FILE BIOSIS
 10 FILES SEARCHED...
        1 FILE BIOTECHNO
  13 FILES SEARCHED...
         5
             FILE CAPLUS
         18
              FILE DDFU
 23 FILES SEARCHED...
         37
             FILE DRUGU
         2
              FILE EMBAL
         36
              FILE EMBASE
         4
             FILE ESBIOBASE
 32 FILES SEARCHED...
          1
              FILE FSTA
              FILE IFIPAT
          3
              FILE JICST-EPLUS
             FILE LIFESCI
          1
 43 FILES SEARCHED...
        30
             FILE MEDLINE
         9
              FILE PASCAL
 48 FILES SEARCHED...
        12
             FILE PHIN
         27
              FILE PROMT
         20
              FILE SCISEARCH
         7
              FILE TOXLINE
 55 FILES SEARCHED...
              FILE TOXLIT
         4
         30
              FILE USPATFULL
        14
              FILE WPIDS
    FILES SEARCHED...
        14
              FILE WPINDEX
```

59 FILES SEARCHED IN STNINDEX

24 FILES HAVE ONE OR MORE ANSWERS,

32 FILES SEARCHED...

```
=> s 110 (w) 111
              FILE ADISALERTS
           3
           2
               FILE BIOSIS
   8 FILES SEARCHED...
  13 FILES SEARCHED...
              FILE CAPLUS
          1
               FILE DDFU
           1
  23 FILES SEARCHED...
              FILE DRUGU
           1
           1
               FILE EMBAL
               FILE EMBASE
           1
               FILE ESBIOBASE
  32 FILES SEARCHED...
           1
              FILE FSTA
               FILE IFIPAT
               FILE LIFESCI
  42 FILES SEARCHED...
  48 FILES SEARCHED...
          1 FILE PROMT
              FILE SCISEARCH
           1
              FILE TOXLINE
           1
  55 FILES SEARCHED...
              FILE USPATFULL
           1
               FILE WPIDS
           3
  58 FILES SEARCHED...
              FILE WPINDEX
  17 FILES HAVE ONE OR MORE ANSWERS, 59 FILES SEARCHED IN STNINDEX
L13 QUE L10 (W) L11
=> d rank
                  ADISALERTS
              3
F2
                  WPIDS
              3
F3
                  WPINDEX
F4
              2
                  BIOSIS
F5
              1
                  CAPLUS
F6
              1
                  DDFU
F7
              1
                  DRUGU
F8
             1
                  EMBAL
F9
              1
                  EMBASE
F10
              1
                  ESBIOBASE
F11
             1
                  FSTA
           . 1
F12 .. .
                  IFIPAT
             1
F13
                  LIFESCI
F14
             1
                 PROMT
F15
             1
                  SCISEARCH
F16
             1
                  TOXLINE
F17
             1
                  USPATFULL
=> d rank 112
'FULL' IS NOT VALID IN THE CURRENT FILE
This option is not valid in the current file. Enter the command
without the option at the arrow prompt (=>). Or, first enter the file in which the saved item created. Then enter the command and
option at an arrow prompt in the file.
```

# => d 112 rank

L12 QUE L10 (S) L11

'FULL' IS NOT VALID IN THE CURRENT FILE

This option is not valid in the current file. Enter the command without the option at the arrow prompt (=>). Or, first enter the file in which the saved item created. Then enter the command and option at an arrow prompt in the file.

=> fil f1-17
COST IN U.S. DOLLARS
SINCE FILE TOTAL
ENTRY SESSION
FULL ESTIMATED COST
12.60
156.47

```
FILE 'ADISALERTS' ENTERED AT 14:16:28 ON 25 MAY 2001
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FILE 'WPIDS' ENTERED AT 14:16:28 ON 25 MAY 2001
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FILE 'WPINDEX' ACCESS NOT AUTHORIZED
FILE 'BIOSIS' ENTERED AT 14:16:28 ON 25 MAY 2001
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FILE 'LIFESCI' ENTERED AT 14:16:28 ON 25 MAY 2001
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FILE 'PROMT' ENTERED AT 14:16:28 ON 25 MAY 2001
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FILE 'SCISEARCH' ENTERED AT 14:16:28 ON 25 MAY 2001
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FILE 'TOXLINE' ENTERED AT 14:16:28 ON 25 MAY 2001
                                                             FILE 'USPATFULL' ENTERED AT 14:16:28 ON 25 MAY 2001
CA INDEXING COPYRIGHT (C) 2001 AMERICAN CHEMICAL SOCIETY (ACS)
=> s 112
   2 FILES SEARCHED...
   5 FILES SEARCHED...
   8 FILES SEARCHED...
  12 FILES SEARCHED...
  14 FILES SEARCHED...
L14
           214 L12
=> s 113
   2 FILES SEARCHED...
   4 FILES SEARCHED...
   7 FILES SEARCHED...
  11 FILES SEARCHED...
  14 FILES SEARCHED...
L15
            20 L13
=> dup rem 115
PROCESSING COMPLETED FOR L15
             13 DUP REM L15 (7 DUPLICATES REMOVED)
L16
```

=> d ibib abs kwic 1-5

L16 ANSWER 1 OF 13 BIOSIS COPYRIGHT 2001 BIOSIS DUPLICATE 1

ACCESSION NUMBER: 2001:228065 BIOSIS DOCUMENT NUMBER: PREV200100228065

TITLE: Low-dose metoprolol CR/XL and fluvastatin slow progression

of carotid intima-media thickness: Main results from the \*\*\*beta\*\*\* - \*\*\*Blocker\*\*\* \*\*\*Cholesterol\*\*\* -

\*\*\*Lowering\*\*\* Asymptomatic Plaque Study (BCAPS. Hedblad, B.; Wikstrand, J.; Janzon, L.; Wedel, H.;

Berglund, G. (1)

CORPORATE SOURCE: (1) Department of Medicine, Malmo University Hospital, S

205 02, Malmo: Goran.Berglund@medforsk.mas.lu.se Sweden

SOURCE: Circulation, (April 3, 2001) Vol. 103, No. 13, pp.

1721-1726. print. ISSN: 0009-7322.

DOCUMENT TYPE: Article
LANGUAGE: English
SUMMARY LANGUAGE: English

AUTHOR(S):

AB Background: Statins reduce cardiovascular events and progression of carotid intima-media thickness (IMT). beta-Blockers are also known to reduce cardiovascular events, but less is known about their effects on carotid IMT. Methods and Results: We conducted a randomized, double-blind, placebo-controlled, single-center trial to compare the effects of low-dose metoprolol CR/XL (25 mg once daily) and fluvastatin (40 mg once daily) on the progression of carotid IMT during 36 months of treatment in 793

subjects who had carotid plaque but no symptoms of carotid artery disease. Changes in mean IMT in the common carotid artery and maximal IMT in the bulb were the main outcome variables. Death and cardiovascular events were monitored. Progression of IMTmax in the carotid bulb at both 18 and 36 . months was reduced by metoprolol CR/XL (-0.058 mm/y; 95% CI, -0.094 to -0.023; P=0.004; and -0.023 mm/y; 95% CI, -0.044 to -0.003; P=0.014, respectively). Incidence of cardiovascular events tended to be lower in metoprolol CR/XL-treated patients (5 versus 13 patients, P=0.055). Rate of IMTmean progression in the common carotid at 36 months was reduced by fluvastatin (-0.009 mm/y; 95% CI, -0.015 to -0.003; P=0.002). Women in the fluvastatin group had increased frequency of transiently high liver enzymes. Conclusions: This is the first randomized trial to show that a beta-blocker can reduce the rate of progression of carotid IMT in clinically healthy, symptom-free subjects with carotid plaque. This suggests that beta-blockers may have a favorable effect on atherosclerosis development.

TI Low-dose metoprolol CR/XL and fluvastatin slow progression of carotid intima-media thickness: Main results from the \*\*\*beta\*\*\* - \*\*\*Blocker\*\*\* \*\*\*Cholesterol\*\*\* - \*\*\*Lowering\*\*\* Asymptomatic Plaque Study (BCAPS.

L16 ANSWER 2 OF 13 ADISALERTS COPYRIGHT 2001 (ADIS)

ACCESSION NUMBER: 2001:7697 ADISALERTS

DOCUMENT NUMBER:

800863000

TITLE:

Low-dose metoprolol CR/XL and fluvastatin show progression of carotid intima- media thickness: main results from the \*\*\*beta\*\*\* - \*\*\*Blocker\*\*\* \*\*\*Cholesterol\*\*\* - \*\*\*lowering\*\*\* Asymptomatic Plaque Study (BCAPS)
ADIS TITLE: Metoprolol vs fluvastatin: therapeutic use.;
Atherosclerosis; Effects on carotid intima-media thickness:

the BCAPS

AUTHOR:

Hedblad B; Wikstrand J; Janzon L; Wedel H; Berglund G

CORPORATE SOURCE: Malmo University Hospital, Malmo, Sweden

SOURCE:

Circulation Circulation 103: 1721 1726, 3 Apr 2001. (Apr 3,

2001)

DOCUMENT TYPE:

(Clinical study)

REFERENCE: Hype

Hyperlipidaemia (Summary): Alert no. 5, 2001

FILE SEGMENT: Summary LANGUAGE: English WORD COUNT: 761

TI Low-dose metoprolol CR/XL and fluvastatin show progression of carotid intima- media thickness: main results from the \*\*\*beta\*\*\* -

\*\*\*Blocker\*\*\* \*\*\*Cholesterol\*\*\* - \*\*\*lowering\*\*\* Asymptomatic

Plaque Study (BCAPS)

ADIS TITLE: Metoprolol vs fluvastatin: therapeutic use.; Atherosclerosis; Effects on carotid intima-media thickness: the BCAPS

TX. . . lack of data concerning the effects of beta- adrenoreceptor antagonists [beta-blockers] on the progression of carotid artery IMT in

humans.

The \*\*\*beta\*\*\* - \*\*\*Blocker\*\*\* \*\*\*Cholesterol\*\*\* -

\*\*\*Lowering\*\*\* Asymptomatic Plaque Study (BCAPS) compared the effects of the beta-adrenoceptor antagonist metoprolol CR/XL [extended release] and the HMG-CoA reductase inhibitor. . .

L16 ANSWER 3 OF 13 TOXLINE

ACCESSION NUMBER: 1999:169015 TOXLINE

DOCUMENT NUMBER: IPA-99-1179444

Cardiovascular risk reduction through promotion of the ABCS TITLE:

in ischemic heart disease in a veteran population.

Abstract of Meeting Presentation COMMENT:

Liao M M; Huynh K C; Gray D R; Hagar J M AUTHOR:

CORPORATE SOURCE: Veterans Affairs Medical Center (119), 5901 East Seventh

Street, Long Beach, CA 90822, USA Internet: . mliao2l@hotmai

ASHP Midyear Clinical Meeting, (1999). Vol. 34, Dec PP-150D SOURCE:

(REF).

FILE SEGMENT: ΙPΑ LANGUAGE: English

OTHER SOURCE: IPA 36-1179444

ENTRY MONTH: 199911

IPA COPYRIGHT: ASHP The risk for recurrent cardiovascular event can be reduced through pharmacotherapy and lifestyle modifications described by the ABCS: aspirin; angiotensin converting enzyme inhibitors; \*\*\*beta\*\*\* - \*\*\*blockers\*\*\* ; \*\*\*cholesterol\*\*\* \*\*\*lowering\*\*\* agents; smoking cessation. Despite evidence supporting lower morbidity and mortality while adhering to the ABCS, there is a large gap between recommended and implemented treatments. The objectives of this randomized, prospective study are to evaluate current adherence with the ABCS in both the cardiology and primary care clinic, develop and implement an assist model that will shorten the treatment gap, and evaluate the impact of the program on treatment compliance. Fifty patients with coronary artery disease were randomly selected using computer generated ICD9 codes. Baseline adherence to the ABCS was similar to the national average. After implementing the assist model, pharmacotherapy was optimized.

. . . recurrent cardiovascular event can be reduced through AΒ pharmacotherapy and lifestyle modifications described by the ABCS: aspirin; angiotensin converting enzyme inhibitors; \*\*\*beta\*\*\* -\*\*\*blockers\*\*\* ; \*\*\*cholesterol\*\*\* \*\*\*lowering\*\*\* agents; smoking cessation. Despite evidence supporting lower morbidity and mortality while adhering to the ABCS, there is a large gap. .

L16 ANSWER 4 OF 13 IFIPAT COPYRIGHT 2001 IFI DUPLICATE 2

ΑN 3223454 IFIPAT; IFIUDB; IFICDB

TITLE: PHARMACEUTICAL PREPARATIONS AND MEDICAMENTS FOR THE

PREVENTION AND TREATMENT OF ENDOTHELIAL DYSFUNCTION; ADMINISTRATION OF 6 MG/KG/DAY OF AN ORGANIC NITRATE TO AN INDIVIDUAL TO MAINTAIN OR IMPROVE ENDOTHELIAL

FUNCTION

INVENTOR(S): Kojda; Georg, Koln, DE

Noack; Eike Albrecht, Neuss, DE ISIS PHARMA GmbH, Zwickau, DE

PATENT ASSIGNEE(S): PRIMARY EXAMINER:

Criares, Theodore J

AGENT: Marshall, O'Toole, Gerstein, Murray & Borun

NUMBER DATE PATENT INFORMATION: US 5973011 19991026 APPLICATION INFORMATION: US 1996-721465 19960927 27 Sep 2016 EXPIRATION DATE:

NUMBER PRIORITY APPLN. INFO.:

DE 1994-4410997 19940330 DE 1995-DE421 19950328 US 5973011 19991026 US 5973011 FAMILY INFORMATION:

DOCUMENT TYPE: UTILITY FILE SEGMENT: CHEMICAL

MICROFILM REEL NO: NUMBER OF CLAIMS: 008336 FRAME NO: 0823

The present invention describes the use of nitric-oxideliberating or

transferring compounds, stimulators of endogenous NO formation, as well as stimulators of guanylate cyclase, for prevention, treatment and elimination of endothelial dysfunctions and the diseases accompanying these dysfunctions or caused by them, as well as the use of said compounds to produce pharmaceutical products for the cited areas of application.

CLMN '

. . . 4 wherein the active compound to treat cardiovascular diseases is selected from the group consisting of ACE inhibitors, antiatherosclerotics, antihypertensives, \*\*\*beta\*\*\* - \*\*\*blockers\*\*\*, \*\*\*cholesterol\*\*\* \*\*\*reducers\*\*\*, diuretics, calcium antagonists, coronary dilators, lipid reducers, peripheral vasodilators and thrombocyte aggregation inhibitors.

L16 ANSWER 5 OF 13 WPIDS COPYRIGHT 2001 DERWENT INFORMATION LTD

ACCESSION NUMBER: 1999-121439 [10] WPIDS

DOC. NO. CPI:

C1999-035644

TITLE:

New nitric acid ester derivatives of pentaerythritol - useful as vasodilators, endothelial protective or platelet aggregation inhibiting agents, and as agents against oxidative stress.

DERWENT CLASS:

B03 B05

INVENTOR(S):

CAWELLO, A; DREWS, R; MEESE, C O; PAAR, F

PATENT ASSIGNEE(S):

(ISIS-N) ISIS PHARMA GMBH; (SCHW-N) SCHWARZ PHARMA AG

COUNTRY COUNT: 8:

PATENT INFORMATION:

PATENT NO	KIND	DATE	WEEK	LA	PG
ZA 9809357 DE 19745622		19981230 19990422	(199910) * (199922)		38

WO 9920638 A1 19990429 (199924) GE

RW: AT BE CH CY DE DK EA ES FI FR GB GH GM GR IE IT KE LS LU MC MW NL OA PT SD SE SZ UG ZW

W: AL AM AT AU AZ BA BB BG BR BY CA CH CN CU CZ DE DK EE ES FI GB GD GE GH GM HR HU ID IL IS JP KE KG KP KR KZ LC LK LR LS LT LU LV MD MG MK MN MW MX NO NZ PL PT RO RU SD SE SG SI SK SL TJ TM TR TT UA UG US UZ VN YU ZW

AU 9915548 A 19990510 (199938)

EP 1023307 A1 20000802 (200038) EN

R: AL AT BE CH CY DE DK ES FI FR GB GR IE IT LI LT LU LV MC MK NL PT RO SE SI

DE 19881521 T 20001012 (200052)

#### APPLICATION DETAILS:

PAT	TENT NO	KIND		API	PLICATION	DATE
ZA	9809357	Α		za	1998-9357	19981014
DE	19745622	A1		DE	1997-19745622	19971016
WO	9920638	A1		WO	1998-DE3031	19981016
ΑU	9915548	Α	•	AU	1999-15548	19981016
ΕP	1023307	A1		ΕP	1998-959730	19981016
				WO	1998-DE3031	19981016
DE	19881521	T		DE	1998-19881521	19981016
				WO	1998-DE3031	19981016

#### FILING DETAILS:

PATENT NO	KIND	PATENT NO
AU 9915548	A Based on	WO 9920638
EP 1023307	Al Based on	WO 9920638
DE 19881521	T Based on	WO 9920638

PRIORITY APPLN. INFO: DE 1997-19745622 19971016

AN 1999-121439 [10] WPIDS

AB ZA 9809357 A UPAB: 19990310

Nitric acid ester derivatives of pentaerythritol of formula (R1)(R2)C(R3)-ONO2 (I) are new: R1-R3 = CH2-ONO2, CH2-OR4 or CH2-R5; and at least 1 of R1-R3 = CH2-R5; R4 = H or 1-3C alkanoyl; R5 = glycoside radical having the alpha - or beta -configuration on C-1 of a

monosaccharide optionally with 1-3C alkanoic or mineral acid fully or partly O-acylated; a uronic acid optionally with 1 3C alkanoic or mineral acid fully or partly O-acylated; a 1-3C alkyluronic acid ester optionally with 1-3C alkanoic or mineral acid fully or partly O-acylated. Use of (I) and compositions containing (I) are also claimed. USE - (I) are as vasodilators, endothelial protective or platelet-aggregation inhibiting agents, and as agents against oxidative stress in vessels and tissues. (I) can be used in combination with known cardiovascular therapeutic agents, e.g. ACE inhibitors, anti-atherosclerotics, anti hypertensives, \*\*\*beta\*\*\* \*\*\*blockers\*\*\* , \*\*\*cholesterol\*\*\* - \*\*\*lowering\*\*\* agents, diuretics, calcium antagonists, coronary dilators, lipid-lowering agents, peripheral vasodilators or platelet aggregation inhibitors. (I) are also useful in chemical synthesis and analysis. Dwg.0/0 vessels and tissues. (I) can be used in combination with known cardiovascular therapeutic agents, e.g. ACE inhibitors, anti-atherosclerotics, anti hypertensives, \*\*\*beta\*\*\* \*\*\*blockers\*\*\* , \*\*\*cholesterol\*\*\* - \*\*\*lowering\*\*\* agents,

AΒ

diuretics, calcium antagonists, coronary dilators, lipid-lowering agents, peripheral vasodilators or platelet aggregation inhibitors. (I) are also useful in chemical. . .

### => d ibib abs kwic 6-13

L16 ANSWER 6 OF 13 WPIDS COPYRIGHT 2001 DERWENT INFORMATION LTD

ACCESSION NUMBER: 1999-010294 [01] WPIDS

C1999-003509 DOC. NO. CPI:

TITLE: Pentaerythritol derivatives - are useful as vasodilating

agents, endothelium-protective agents or platelet

aggregation-inhibiting agents.

DERWENT CLASS: B03 B05

INVENTOR(S): BROSIG, H; HESS, U; KOENIG, G; WINDECK, A

(ISIS-N) ISIS PHARMA GMBH PATENT ASSIGNEE(S):

SK 9901695 A3 20001107 (200102)

PATENT NO KIND DATE WEEK LA PG

COUNTRY COUNT:

PATENT INFORMATION:

ZA	980	5064	1	Α	19	981	1028	(]	1999	901)	* [	ΞN	42	2									
DE	1982	2678	31	A1	19	981	1217	' (1	1999	905)													
WO	9850	5759	9	A2	2 19	981	1217	(1	1999	905)	(	GΕ											
	RW:	ΑT	BE	CH	CY	DE	DK	EΑ	ES	FΙ	FR	GB	GH	GM	GR	ΙE	ΙT	ΚE	LS	LU	MC	WM	NL
							UG																
	₩:	AL	ΑM	ΑT	ΑU	ΑZ	BA	ВB	ВG	BR	BY	CA	СН	CN	CÜ	CZ	DE	DK	EΕ	ES	FΙ	GB	GΕ
		GH	GΜ	GW	HU	ΙD	$_{ m IL}$	IS	JP	ΚE	KG	ΚP	KR	ΚZ	LC	LK	LR	LS	$_{ m LT}$	LU	LV	MD	MG
		MK	MN	MW	MΧ	NO	NZ;	PL	PT	RO	RU	SD	SE	SG	SI	SK	$\mathtt{SL}$	TJ	TM	TR	TT	UA	UG
		US	UZ	VN	YU	zw																	
ΑU	988	5321	L	Α	19	981	1230	) (]	1999	920)													
NO	990	5128	3	Α	19	9991	1210	(2	2000	016)													
EΡ	9882	282		A2	2 20	0000	329	(2	2000	020)	(	ΞE											
	R:	AL	ΑT	ΒE	CH	CY	DE	DK	ES	FΙ	FR	GB	GR	ΙE	ΙT	LI	LΤ	LU	$L\Lambda$	MC	MK.	NL	PT
		RO	SE	SI																			
	1988			T				-															
CN	126	6429	9	Α	20	0000	913	3 (2	2000	062)	)												

## APPLICATION DETAILS:

PAT	TENT NO	KIND			PLICATION	DATE		
DE	9805064 19826781 9856759	A A1 A2		DE	1998-5064 1998-19826781 1998-DE1635	19980611 19980611 19980611		
AU	9885321 9906128	A A		AU	1998-85321 1998-DE1635	19980611 19980611		
EP	988282	A2	`•	EP	1999-6128 1998-936180	19991210 19980611		
DE	19880813	T			1998-DE1635 1998-19880813	19980611 19980611		

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WO 1998-DE1635
                                                        19980611
                                       CN 1998-808056
                                                        19980611
     CN 1266429
                  A3
                                       WO 1998-DE1635
                                                        19980611
     SK 9901695
                                                        19980611
                                       SK 1999-1695
FILING DETAILS:
     PATENT NO KIND
                                      PATENT NO
     _____
    AU 9885321 A Based on WO 9856759
EP 988282 A2 Based on WO 9856759
    DE 19880813 T Based on
                                     WO 9856759
PRIORITY APPLN. INFO: DE 1997-19725340 19970611
    1999-010294 [01] WPIDS
         9805064 A UPAB: 19990107
     Pentaerythritol derivatives of formula (I), (III), (VI), (VII), (VIII) and
     (XV) and their salts are new: (O2NOCH2)mC(CH2OH)n(CH2COR1)o(COR1)p
     (O2NOCH2) mC (CH2OH) n (CH2COR3) o (COR3) p
                                            (III)
                                              (VI) (HOCH2)q(O2NOCH2)rC(CH2OR6)s
     (O2NOCH2) mC (CH2OH) n (CH2COR5) o (COR5) p
     (VII) (O2NOCH2) mC (CH2OH) n (CH2COR7) o (COR7) p
                                                    (VIII)
     (HOCH2)q(O2NOCH2)rC(CH2OR14)s (XV) R1 = a group of formula (II); R3 =
     a group of formula (IV); R5 = (2-carboxyphenyl)oxy or (2-
     alkoxycarbonylphenyl)oxy; R6 = salicyloyl or acetylsalicyloyl; R7 = a
     group of formula (IX); R14 = acyl radical of a compound of formula (X),
     (XI), (XII), (XIII) or (XIV) (sic); R2 = 1-20C alkyl, especially Me, Et,
     n-Pr, i-Pr, n-butyl, n-pentyl, n-hexyl, n-octyl, benzyl, cyclohexylmethyl,
     4-chlorobenzyl, 4-nitrobenzyl, 2-phenylethyl, 3-phenylpropyl,
     3-cyclohexylpropyl, 3-phthalimidylpropyl, 1-naphthylmethyl, cinnamyl,
     5-ethoxycarbonylbutyl, 3-aminopropyl, -(CH2)3CH(NHCOCH3)COOH,
     -(CH2)3CH(NHCOCH3)COOCH3 or 1,6-hexane-bis; R8, R9 = 1-6C alkyl or R8+R9 =
     1-6C alkylene; R10 = OH, NHR8R9, 1-6C alkoxy, (2-carboxyphenyl)oxy,
     (2-alkoxycarbonylphenyl)oxy, (1-carboxymethyl-2-dialkylamino)ethoxy,
     (1-carboxymethyl-2-trialkylammonium)ethoxy, (1-alkoxycarbonylmethyl-2-
     dialkylamino)ethoxy or (1-alkoxycarbonylmethyl-2-trialkylammonium)ethoxy;
    m, p, r, s at least 1; m+n+o+p=4; q+r+s=4. Also claimed are compounds of formula (V), (X), (XI) and (XIV) and their salts. R4 = H, 1-6C
     alkanoyl, salicyloyl or acetylsalicyloyl; R11 = NO2 and for (XV) H, 1-6C
     alkanoyl, salicyloyl, acetylsalicyloyl or -CO-CH2CH(OH)-CH2-NR8R9; R12 =
     1-6C alkyl, especially Me, Et or n-Pr; R13 = H or 1-6C alkyl; X = an anion
     or absent if COR10 is capable of forming an inner salt.
          USE - (I), (III), (V) and (VI) are useful as vasodilating agents,
     endothelium-protective agents or platelet aggregation-inhibiting agents
     and can be used in combination with other agents (especially ACE
     inhibitors, antiatherosclerotics, antihypertensives,
       ***blockers*** , ***cholesterol*** - ***lowering*** agents,
     diuretics, calcium antagonists, coronary dilators, lipid-lowering agents,
     peripheral vasodilators, phosphodiesterases or platelet aggregation
     inhibitors) for the treatment of cardiovascular or vessel diseases.
     Dwg.0/0
     endothelium-protective agents or platelet aggregation-inhibiting agents
     and can be used in combination with other agents (especially ACE
     inhibitors, antiatherosclerotics, antihypertensives, ***beta***
       ***blockers*** , ***cholesterol*** - ***lowering*** agents,
     diuretics, calcium antagonists, coronary dilators, lipid-lowering agents,
     peripheral vasodilators, phosphodiesterases or platelet aggregation
     inhibitors) for the treatment of cardiovascular.
L16 ANSWER 7 OF 13 WPIDS COPYRIGHT 2001
                                            DERWENT INFORMATION LTD
                                         WPIDS
ACCESSION NUMBER:
                     1998-231501 [21]
CROSS REFERENCE:
                     1998-322290 [28]
DOC. NO. CPI:
                      C1998-072398
                      New pentaerythritol nitrate ester derivatives - useful as
TITLE:
                      explosives and as pharmaceuticals for treating heart and
                      circulatory conditions.
DERWENT CLASS:
                      B05 E19 K04
                      HESS, U; BROSIG, H; WINDECK, A
INVENTOR(S):
                      (ISIS-N) ISIS PHARMA GMBH
PATENT ASSIGNEE(S):
COUNTRY COUNT:
```

AN

AB

ΑB

PATENT INFORMATION:

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PATENT NO KIND DATE WEEK LA PG

DE 19641667 A1 19980416 (199821)* 7

NO 9901622 A 19990604 (199932)

CN 1239944 A 19991229 (200019)

SK 9900434 A3 20000214 (200020)
```

#### APPLICATION DETAILS:

P.	ATENT NO	KIND	APPLICATION	DATE
D D	E 19641667	A1	DE 1996-19641667	19961010
N	0 9901622	Α	WO 1997-DE2328	19971010
			NO 1999-1622	19990406
С	N 1239944	Α	CN 1997-180509	19971010
S	K 9900434	A3	WO 1997-DE2328	19971010
			SK 1999-434	19971010

PRIORITY APPLN. INFO: DE 1996-19641667 19961010; DE 1996-19652345 19961217; DE 1997-19726812 19970625

AN 1998-231501 [21] WPIDS

CR 1998-322290 [28]

AB DE 19641667 A UPAB: 20000426

Nitrate esters of formula (I)-(III), their salts and compounds of formula (IV) are new. In (I), R1-R3 = H, OR6, ONO2, OR4 or R5; R4 = COR6 or R10; R5 = PO4R7, PO4R9, SO3R9 or COOR6; R6 = H or 1-6C alkyl; R7 = 1-6C alkylene-R8; R8 = N(R6)2, N+(R6)3 or N+(R6)3 X-; R9 = R6, aryl or N(R6)2; R10 = a 3- or 5-carbonyleresidue of a 2,4 and/or 6-optionally substituted 1,4-dihydropyridine-3,5-dicarboxylic acid; 1-substituted pyrrolidine-2-carbonyl group; an N-carbonyl residue of a substituted sydnoneimine; CO-CH(NHCOR6)-C(R6)2-S-NO; CO-CH(NH2)-C(R6)2-S-NO or NH-CH(COOR6)-C(R6)2-S-NO; X = halogen or an anion-forming group. The following combinations ar excluded: R1-R3 = ONO2; R1 = OH and R2, R3 = ONO2; R1 = R2 = OH and R3 = ONO2; and R1-R3 = OH. In (II), R11 = NO2 acyl, alkyl or alkenyl. In (III), R12 = NO2 or as for R4-R10; n = 0-10. In (IV), each Q is the same and is OH or ONO2.

USE - Pharmaceutical compositions are claimed which contain the above compounds optionally combined with other compounds for the treatment of heart or circulation conditions, especially where the indications are for ACE-inhibitors, anti-atherosclerotics, antihypertensives, \*\*\*beta\*\*\* - \*\*\*blockers\*\*\* , \*\*\*cholesterol\*\*\* \*\*\*lowering\*\*\* agents, diuretics, calcium antagonists, coronary dilators, lipid lowering agents, peripheral vasodilators, or thrombocyte aggregation inhibitors (all claimed). Explosive mixtures containing the compounds are also claimed.

ADVANTAGE - The compounds have improved activity and reduced side effects.

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with other compounds for the treatment of heart or circulation conditions, especially where the indications are for ACE-inhibitors, anti-atherosclerotics, antihypertensives, \*\*\*beta\*\*\* - \*\*\*blockers\*\*\*, \*\*\*cholesterol\*\*\* \*\*\*lowering\*\*\* agents, diuretics, calcium antagonists, coronary dilators, lipid lowering agents, peripheral vasodilators, or thrombocyte aggregation inhibitors (all claimed). Explosive mixtures containing. . .

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L16 ANSWER 8 OF 13 FSTA COPYRIGHT 2001 IFIS
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ACCESSION NUMBER: 1999(04):H0648 FSTA FS FSTA

TITLE: Alcohol in the myocardial infarction patient.

AUTHOR: Criqui, M.

CORPORATE SOURCE: Dep. of Family & Preventive Med., Univ. of California,

San Diego, La Jolla, CA 92093, USA

SOURCE: Lancet, (1998) 352 (9144) 1873, 8 ref.

ISSN: 0140-6736.

DOCUMENT TYPE:

LANGUAGE:

Journal English

AB The study conducted by Muntwyler et al. [See 1999-Ha642], showing decreased mortality as a result of moderate alcoholic beverage consumption in men who have previously had a myocardial infarction, is critically discussed. Aspects considered include: the relatively high reduction in risk of death from non-cardiovascular disease; possible uncontrolled

confounding by lifestyle, medicines or other factors; problems with the selected nature of people participating in cohort studies; the lack of consideration of interaction of alcohol consumption with factors such as .

\*\*\*beta\*\*\* .- \*\*\*blockers\*\*\* , \*\*\*cholesterol\*\*\* - \*\*\*reducing\*\*\*
medicines or aspirin; and problems with low acceptability of use of alcohol as a cardioprotective agent, because of adverse effects of alcohol

AB . . . nature of people participating in cohort studies; the lack of consideration of interaction of alcohol consumption with factors such as .

\*\*\*beta\*\*\* .- \*\*\*blockers\*\*\* , \*\*\*cholesterol\*\*\* - \*\*\*reducing\*\*\* medicines or aspirin; and problems with low acceptability of use of alcohol as a cardioprotective agent, because of adverse effects. . .

L16 ANSWER 9 OF 13 LIFESCI COPYRIGHT 2001 CSA

ACCESSION NUMBER: 1998:100592 LIFESCI

TITLE: Gene therapy for therapeutic myocardial angiogenesis: A

promising synthesis of two emerging technologies

AUTHOR: Lee, J.S.; Feldman, A.M.

CORPORATE SOURCE: University of Pittsburgh Heart Institute, G324, PUH, 200

Lothrop Street, Pittsburgh, PA 15213, USA

SOURCE: Nat. Med., (19980600) vol. 4, no. 6, pp. 739-741.

ISSN: 1078-8956.

DOCUMENT TYPE: Journal

TREATMENT CODE: General Review

FILE SEGMENT: W3
LANGUAGE: English
SUMMARY LANGUAGE: English

Ischemic heart disease due to atherosclerotic narrowing or occlusion of the coronary arteries affects 15 to 20 million Americans and remains the leading cause of death in developed countries. Despite remarkable advances in mechanical (for example, percutaneous angioplasty, stent implantation, bypass surgery) and medical therapy (for example, \*\*\*beta\*\*\* \*\*\*blockers\*\*\* , \*\*\*cholesterol\*\*\* \*\*\*lowering\*\*\* anti-thrombotic agents) of atherosclerotic disease, a large number of patients remain symptomatic because of inadequacies in and limitations of these approaches. Recently, investigators have tested the hypotheses that the ischemia could be attenuated or abrogated by therapeutic angiogenesis. Therapeutic angiogenesis, by stimulating the growth of new vessels that collateralize the affected vessel, in effect producing an auto-bypass of the narrowing or blockage, represents a theoretically attractive and intuitively rational new approach to the problem. Not surprisingly, these efforts have received a large amount of attention from the press, the scientific community, as well as the business community. Although basic research in the field of angiogenesis has provided several potential biologic agents for stimulating vessel growth, significant technical barriers remain in terms of safe and practical local delivery of these agents to the ischemic myocardium. However, recent research efforts have demonstrated that gene therapy may offer unique solutions to these barriers, producing a promising union of two rapidly developing - but relatively untested - fields, and bringing therapeutic angiogenesis in humans one step closer to reality.

AB . . . developed countries. Despite remarkable advances in mechanical (for example, percutaneous angioplasty, stent implantation, bypass surgery) and medical therapy (for example, \*\*\*beta\*\*\* - \*\*\*blockers\*\*\*, \*\*\*cholesterol\*\*\* \*\*\*lowering\*\*\* agents, anti-thrombotic agents) of atherosclerotic disease, a large number of patients remain symptomatic because of inadequacies in and limitations of . . .

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L16 ANSWER 10 OF 13 ADISALERTS COPYRIGHT 2001 (ADIS)
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ACCESSION NUMBER: 1999:16509 ADISALERTS

DOCUMENT NUMBER: 800737937

TITLE: Quality of life in the \*\*\*Beta\*\*\* - \*\*\*blocker\*\*\*

\*\*\*Cholesterol\*\*\* - \*\*\*lowering\*\*\* Asymptomatic Plaque

Study

AUTHOR: Hedner E; Halling K

SOURCE: Quality of Life Research (Nov 1, 1998), Vol. 7, pp. 605-606

DOCUMENT TYPE: (Clinical study); Abstract

REFERENCE: Hyperlipidaemia (Index only): Alert no. 4, 1999;
PharmacoEconomics (Index only): Alert no. 4, 1999

FILE SEGMENT: Citation LANGUAGE: English

[I] Quality of life in the \*\*\*Beta\*\*\* - \*\*\*blocker\*\*\*

\*\*\*Cholesterol\*\*\* - \*\*\*lowering\*\*\* Asymptomatic Plaque Study

L16 ANSWER 11 OF 13 PROMT COPYRIGHT 2001 Gale Group

ACCESSION NUMBER: 97:246477 PROMT

Noncompliance "Will Cost US Firms \$25 Bill In 1997" TITLE:

Marketletter, (5 May 1997) pp. N/A. SOURCE:

ISSN: 0951-3175.

LANGUAGE: English WORD COUNT: 603

\*FULL TEXT IS AVAILABLE IN THE ALL FORMAT\*

Arthritis sufferers are the leading patient group not refilling their prescriptions, says Xpand Rx, a new IMS database product which measures prescribed drug therapy patient noncompliance. IMS marketing vice president Bob Merrold said the data showed almost 70% of all antiarthritic prescriptions are never refilled, and that of the prescriptions that are refilled, the average patient takes 50% too long to obtain the refill. Failure to follow prescribed therapy regimens is common in many leading therapeutic classes, IMS data shows. Others in the top 10 noncompliance rankings are estrogen/progesterones, antispasmodics, selective serotonin

reuptake inhibitors, \*\*\*beta\*\*\* \*\*\*blockers\*\*\* ,

\*\*\*cholesterol\*\*\* \*\*\*reducers\*\*\* , ACE inhibitors, calcium blockers, oral estrogens and benzodiazepine tranquilizers. These categories ranked above or just below 50% in nonpersistence, which IMS defines as prescription refills not actually bought. Antiarthritics, antispasmodics, SSRIs, cholesterol reducers, oral estrogens and benzodiazepines all exceeded 20% in noncompliance or additional time taken to consume purchased prescriptions.

Xpand Rx data puts individual-company lost revenues due to nonpersistence over \$1 billion a year, and revenues lost to the industry due to all types of noncompliance at \$25 billion this year. Noncompliance also costs \$100 billion in health care and productivity, notes a recent report. While managed care is dominant in many US states, it still pays for under half the prescriptions in 21 states. IMS' Retail Method-of-Payment Report says third-party managed-care sources accounted for \$42.5 billion, or 58.5%, of all retail drug sales in 1996, cash payments made up 29.3% and Medicaid 12.3%. Third-party sources led, with 55% of all dispensed prescriptions (1.2 billion) for the full year, with cash sources accounting for 33.4% and Medicaid for 11.6%. 1996 was the first year that third-party sources accounted for over half of all prescriptions. IMS found that in 29 states over various regions, non-government managed care paid for over half of all retail prescriptions. In states with the highest managedcare percentages (mainly on the East Coast or in the Southwest) the number of prescriptions paid by managed-care organizations was 61%-75%. 21 states had managed-care penetration of under 50%, and the lowest states (eg Alaska, the Dakotas, Montana, Arkansas and Mississippi) had managed-care shares under 40%.

THIS IS AN EXCERPT: COPYRIGHT 1997 Marketletter Publications Ltd. (UK) Failure . . . leading therapeutic classes, IMS data shows. Others in the top 10 noncompliance rankings are estrogen/progesterones, antispasmodics, selective serotonin reuptake inhibitors, \*\*\*beta\*\*\* \*\*\*blockers\*\*\* , \*\*\*cholesterol\*\*\* \*\*\*reducers\*\*\* , ACE inhibitors, calcium blockers, oral estrogens and benzodiazepine tranquilizers. These categories ranked above or just below 50% in nonpersistence, which.

TXFailure . . . leading therapeutic classes, IMS data shows. Others in the top 10 noncompliance rankings are estrogen/progesterones, antispasmodics, selective serotonin reuptake inhibitors, \*\*\*beta\*\*\* \*\*\*blockers\*\*\* , \*\*\*cholesterol\*\*\* \*\*\*reducers\*\*\* , ACE inhibitors, calcium blockers, oral estrogens and benzodiazepine tranquilizers. These categories ranked above or just below 50% in nonpersistence, which.

L16 ANSWER 12 OF 13 ADISALERTS COPYRIGHT 2001 (ADIS)

ACCESSION NUMBER: 1997:65993 ADISALERTS

DOCUMENT NUMBER: 800653365

TITLE: Is there a role for antioxidant vitamins in the prevention of cardiovascular diseases? An update on epidemiological and clinical trials data ADIS TITLE: Ascorbic acid, betacarotene, tocopherol: therapeutic use.; Prevention of cardiovascular disorders; Review (37 references)

Lonn E M; Yusuf S AUTHOR:

CORPORATE SOURCE: McMaster University, Hamilton, Ontario, Canada

Canadian Journal of Cardiology (Oct 1, 1997), Vol. 13, pp. SOURCE:

957-965

DOCUMENT TYPE: General Review

Ischaemic Heart Disease (Summary): Alert no. 1, 1998 REFERENCE:

Summary FILE SEGMENT: English LANGUAGE:

325 WORD COUNT:

. . clinical benefit are recommended. 'These include smoking cessation, a heart-healthy diet, regular exercise and drug therapies such as

acetylsalicylic acid, \*\*\*beta\*\*\* - \*\*\*blockers\*\*\* ,
 \*\*\*cholesterol\*\*\* - \*\*\*lowering\*\*\* drugs, blood pressure-lowering drugs and angiotensin-converting inhibitors in specific high risk patient groups.'

L16 ANSWER 13 OF 13 BIOSIS COPYRIGHT 2001 BIOSIS

ACCESSION NUMBER: 1992:372200 BIOSIS

DOCUMENT NUMBER: BA94:54250

EFFECTS OF VARIOUS DRUGS ON SECONDARY PREVENTION OF TITLE:

MYOCARDIAL INFARCTION.

ISHIKAWA K; KANAMASA K; HAMA J; OGAWA I; YAMASHITA K; AUTHOR(S):

TAKENAKA T; NAITO T; MIYAZAKI T; KAMATA N; ET AL

FIRST DEP. INTERN. MED., KINKI UNIV. SCH. MED., OSAKA, CORPORATE SOURCE:

MED J KINKI UNIV, (1992) 17 (1), 9-21. SOURCE:

CODEN: KDIZDD. ISSN: 0385-8367.

FILE SEGMENT: BA; OLD Japanese LANGUAGE:

To examine the efficacy of various drugs to prevent recurrent myocardial infarction, a study was conducted on 1,634 cases with myocardial infarction, who were hospitalized or treated at the out-patient clinic between January 1986 and October 1990. Drugs studied were calcium antagonists, nitrates, antiplatelet agents, beta-blockers, warfarin and cholesterol lowering drugs. The primary endpoint was reinfarction or sudden death. One hundred and seven cases had reinfarction and there were 9 cases with sudden death. The cardiac events were significantly reduced in patients treated with antiplatelet agents among 6 drugs. There were 38 cardiac events in 906 cases (4.2%) in patients treated with antiplatelet agents, while 53 cardiac events in 715 cases (7.4%) in non-treated groups. We consider that the prevention of coronary thrombus formation by antiplatelet agents was effective for secondary prevention of myocardial infarction.

ΙT Miscellaneous Descriptors

WARFARIN ASPIRIN CARDIOVASCULAR-DRUG HEMATOLOGIC-DRUG \*\*\*BLOCKERS\*\*\* \*\*\*CHOLESTEROL\*\*\* \*\*\*LOWERING\*\*\* AGENT

PHARMACODYNAMICS

=> s dosag? or formulat?

1676956 DOSAG? OR FORMULAT? L17

=> s folic or vitamin B

88719 FOLIC OR VITAMIN B L18

=> s 114 (s) 118

2 L14 (S) L18 L19

=> d ibib abs kwic tot

ANSWER 1 OF 2 DRUGU COPYRIGHT 2001 DERWENT INFORMATION LTD

PTBS ACCESSION NUMBER: 1986-22492 DRUGU

Contemporary Recommendations for Evaluating and Treating TITLE:

Hyperlipidemia.

AUTHOR: Perry R S

Fargo, N. Dak., United States LOCATION:

Clin. Pharm. (5, No. 2, 113-27, 1986) 2 Fig. 6 Tab. 134 Ref. SOURCE:

ISSN: 0278-2677 CODEN: CPHADV

College of Pharmacy, North Dakota State University, Fargo, ND AVAIL. OF DOC.:

58105, U.S.A.

LANGUAGE: English

Journal DOCUMENT TYPE:

FIELD AVAIL.: AB; LA; CT
FILE SEGMENT: Literature
AN 1986-22492 DRUGU P T B S

The biochemistry, etiology and evaluation of hyperlipidemia and its treatment are reviewed. Both dietary and drug therapies, with drugs including cholestyramine, colestipol HCl, niacin, probucol, dextrothyroxine Na, neomycin sulfate, clofibrate, gemfibrozil, compactin and mevinolin, are considered. The effects of various drugs on lipid and lipoprotein concentrations and their side effects were discussed.

Evidence supporting the role of increased cholesterol as an independent ABEX risk factor for coronary artery disease has been accumulated, although the role of raised triglyceride concentrations is not certain. Laboratory diagnosis of hyperlipidemia involved repeated measurement of serum or plasma cholesterol and triglyceride. Lipid and lipoprotein concentrations may be adversely affected by p.o. contraceptives, thiazide \*\*\*beta\*\*\* \*\*\*blockers\*\*\* (perhaps counteracted by diuretics and labetalol). Prazosin, Ca antagonists and ACE inhibitors e.g. captopril, enalapril, have not been shown to have any important effects. Phenytoin, terbutaline and benzodiazepines may affect HDL-cholesterol. The aims of therapy include the reduction of cholesterol, triglyceride or both and the minimization of side effects. Most patients can be managed with diet alone. When needed, drugs used include bile-acid-binding resins (cholestyramine and colestipol HCl); vitamin K and \*\*\*folic\*\*\* supplements may be needed. These resins, neomycin, dextrothyroxin, clofibrate and gemfibrozil, may alter the absorption of warfarin, digitoxin, digoxin, thyroxine, thiazides and/or iron. Cholestyramine and dextrothyroxine contain tartrazine and should be used cautiously in aspirin-sensitive patients. There is no difference in the

\*\*\*cholesterol\*\*\* - \*\*\*lowering\*\*\* effects of dextro- and levo-thyroxine. Propranolol has been suggested to control the cardiac effects of dextrothyroxine. Surgery may be required in patients with severe familial hypercholesterolemia who do not respond to diet or drug

therapy. (E25/HLR)

. . serum or plasma cholesterol and triglyceride. Lipid and ABEX. lipoprotein concentrations may be adversely affected by p.o. contraceptives, thiazide diuretics and \*\*\*beta\*\*\* \*\*\*blockers\*\*\* (perhaps counteracted by labetalol). Prazosin, Ca antagonists and ACE inhibitors e.g. captopril, enalapril, have not been shown to have any. can be managed with diet alone. When needed, drugs used include bile-acid-binding resins (cholestyramine and colestipol HCl); vitamin K \*\*\*folic\*\*\* acid supplements may be needed. These resins, neomycin, dextrothyroxin, clofibrate and gemfibrozil, may alter the absorption of warfarin, digitoxin, digoxin, . . iron. Cholestyramine and dextrothyroxine contain tartrazine and should be used cautiously in aspirin-sensitive patients. There is no difference in the \*\*\*cholesterol\*\*\* - \*\*\*lowering\*\*\* effects of dextro- and levo-thyroxine. Propranolol has been suggested to control the cardiac effects of dextrothyroxine. Surgery may be required.

L19 ANSWER 2 OF 2 USPATFULL

ACCESSION NUMBER: 97:118019 USPATFULL

TITLE: Steroidal glycosides as antihyperlipidemic agents

INVENTOR(S): Kim, Dooseop, Westfield, NJ, United States

PATENT ASSIGNEE(S): Merck & Co., Inc., Rahway, NJ, United States (U.S.

corporation)

NUMBER DATE

PATENT INFORMATION: US 5698527 19971216 APPLICATION INFO.: US 1996-688582 19960730 (8)

DOCUMENT TYPE: Utility
PRIMARY EXAMINER: Owens, Amelia

LEGAL REPRESENTATIVE: Quagliato, Carol S; Winokur, Melvin

NUMBER OF CLAIMS: 13
EXEMPLARY CLAIM: 1
LINE COUNT: 1307

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

AB Ergostanone derivatives substituted with dissaccharides are cholesterol absorption inhibitors useful in the treatment of hypercholesterolemia and related disorders. These cholesterol absorption inhibitors may be employed alone or in combination with other cholesterol lowering agents.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

The compounds of this invention may also be administered in combination SUMM with other \*\*\*cholesterol\*\*\* \*\*\*lowering\*\*\* agents such as those which inhibit an enzymatic pathway in the biosynthesis of cholesterol. Examples of additional active agents which. . . (ACAT) inhibitors; probucol; niacin; fibrates such as clofibrate, fenofibrate, and gemfibrizol; bile acid sequestrants; LDL (low density lipoprotein) receptor inducers; \*\*\*vitamin\*\*\* \*\*\*B\*\*\* .sub.6 (also known as pyridoxine) and the pharmaceutically acceptable salts thereof such as the HCl salt; \*\*\*vitamin\*\*\* \*\*\*B\*\*\* .sub.12 (also known as cyanocobalamin); aspirin; \*\*\*beta\*\*\* - \*\*\*blockers\*\*\* ; and anti-oxidant vitamins such as vitamin C and E and beta carotene.

=> s 117 (s) 1148 FILES SEARCHED... 6 L17 (S) L14

=> d ibib abs kwic tot

L20 ANSWER 1 OF 6 WPIDS COPYRIGHT 2001 DERWENT INFORMATION LTD

ACCESSION NUMBER: 2000-500307 [45] WPIDS

DOC. NO. CPI: C2000-150306

Controlled release dosage form for e.g. antiinflammatory TITLE: drug comprises has water permeable coating controlling influx of water to core comprising osmotic agent and low

solubility drug.

A96 B05 B07 DERWENT CLASS:

APPEL, L E; CURATOLO, W J; HERBIG, S M; NIGHTINGALE, J A; INVENTOR(S):

THOMBRE, A G; NIGHTINGALE, J A S

PATENT ASSIGNEE(S): (PFIZ) PFIZER PROD INC

COUNTRY COUNT: 27

PATENT INFORMATION:

PATENT NO KIND DATE WEEK PG

EP 1027888 A2 20000816 (200045)\* EN 29

R: AL AT BE CH CY DE DK ES FI FR GB GR IE IT LI LT LU LV MC MK NL PT RO SE SI

JP 2000229846 A 20000822 (200045) 24 CA 2298238 A1 20000810 (200052) EN

## APPLICATION DETAILS:

PATENT NO K	IND		PLICATION	DATE
	A2		2000-300572	20000126
JP 2000229846	A	JP	2000-33132	20000210
CA 2298238	Δ1	CA	2000-2298238	20000209

PRIORITY APPLN. INFO: US 1999-119406 19990210

AN 2000-500307 [45] WPIDS

AΒ 1027888 A UPAB: 20000918

NOVELTY - Controlled release dosage form comprises:

- (1) a core comprising an osmotic agent and low solubility drug in a solid dispersion in a polymer and
  - (2) a water permeable coating.

The coating controls influx of water to the core from an aqueous environment to extrude at least part of the core through at least one delivery port to the aqueous environment.

DETAILED DESCRIPTION - Controlled release dosage form comprises:

- (1) a core comprising an osmotic agent and a low solubility drug in a solid dispersion in a polymer and
- (2) a water permeable coating around the core having at least one delivery port.

The coating controls influx of water to the core from an aqueous environment to extrude at least part of the core through at least one delivery port to the aqueous environment. The coating is non dissolving and non eroding during release of the drug. At least a major part of the drug is amorphous.

USE - Used for treating diseases and disorders.

ADVANTAGE - The controlled release dosage form delivers a low solubility drug with a short elimination half-life which improves drug bioavailability.

Dwg.0/7

TECH.

drug comprises an antihypertensive, anxiolytic, anticlotting agent, blood glucose lowering agent, antihistamine, antitussive, antiinflammatory, antiarteriosclerotic agent, antipsychotic agent, cognitive enhancer, autoimmune disorders agent, hypnotic agent, anti-Parkinsonism agent, antibiotic, antiviral agent, antiimpotence agent, antineoplastic, sedative, barbiturate, nutritional agent, \*\*\*beta\*\*\* - \*\*\*blocker\*\*\* , emetic, antiemetic, diuretic, anticoagulant, cardiotonic, androgen, corticoid, anabolic agent, antidepression agent, antiinfective agent, coronary vasodilator, carbonic anhydrase inhibitor, antifungal, antiprotozoal,. . . antidepression agent comprises fluotexine, paroxetine, venlafaxine, sertraline, (3,6-dimethyl-2-(2,4,6trimethylphenoxy)-pyridin-4-yl)-(1-ethylpropyl)-amine or 3,5-dimethyl-4-(3'-pentoxy)-2-(2',4',6'-trimethylphenoxy)-pyridine. The glycogen phosphorylase inhibitor comprises (R-(RasteriskSasterisk))-5chloro-N-(2-hydroxy-3-(methoxymethylamino)-3-oxo-1-(phenylmethyl)propyl)propyl)-1H-indole-2-carboxamide or 5-chloro-1H-indole-2-carboxylic acid (1S)-benzyl-3-((3R, 4S)dihydroxypyrrolidin-1-yl)-(2R)-hydroxy-3-oxypropyl)amide. Preferred \*\*\*dosage\*\*\* form: The delivery port comprises pores in the coating or is formed by laser drilling, erosion of a plug of. . water swellable polymer. The osmotic agent is in a first layer and the solid dispersion is in a second layer. \*\*\*dosage\*\*\* form also comprises a solubility enhancing agent comprising e.g. organic acids or their metal salts, glycerides, polyethylene glycol esters, sorbitan esters or carbonate salts. \*\*\*dosage\*\*\* form provides a maximum concentration of the drug in a use environment that is at least 1.2 times that of a control \*\*\*dosage\*\*\* form comprising an identical \*\*\*dosage\*\*\* form containing an equivalent amount of undispersed drug and an area under the curve (AUC) in a use environment that is at least 12.25 times that of a \*\*\*dosage\*\*\* form comprising an identical form containing an equivalent amount of undispersed drug. The \*\*\*dosage\*\*\* form provides a maximum drug concentration in the blood at a tmax which is at least 30 minutes longer but not more than 24 hours longer than the tmax observed for the control \*\*\*dosage\*\*\* form. The environment of use is the gastrointestinal tract.

TECHNOLOGY FOCUS - POLYMERS - The coating is formed from e.g. polyacrylic acids. . .

L20 ANSWER 2 OF 6 WPIDS COPYRIGHT 2001 DERWENT INFORMATION LTD

ACCESSION NUMBER: 2000-492338 [44] WPIDS

DOC. NO. CPI: C2000-148097

TITLE: Controlled release dosage composition for low solubility

drug comprises aqueous soluble cellulosic polymeric

matrix containing solid dispersion of drug in cellulosic

polymer.

DERWENT CLASS: A96 B03 B07

INVENTOR(S): APPEL, L E; CURATOLO, W J; FRIESEN, D T; NIGHTINGALE, J

A; THOMBRE, A G; NIGHTINGALE, J A S

PATENT ASSIGNEE(S): (PFIZ) PFIZER PROD INC

COUNTRY COUNT: 27

PATENT INFORMATION:

PATENT NO KIND DATE WEEK LA PG

EP 1027887 A2 20000816 (200044)\* EN 26

R: AL AT BE CH CY DE DK ES FI FR GB GR IE IT LI LT LU LV MC MK NL PT

RO SE SI

JP 2000229888 A 20000822 (200045) 26

CA 2298245 A1 20000810 (200052) EN

## APPLICATION DETAILS:

PATENT NO KIND APPLICATION DATE

 EP 1027887
 A2
 EP 2000-300546
 20000126

 JP 2000229888
 A
 JP 2000-33446
 20000210

 CA 2298245
 A1
 CA 2000-2298245
 20000209

PRIORITY APPLN. INFO: US 1999-119400 19990210

AN 2000-492338 [44] WPIDS

AB EP 1027887 A UPAB: 20000913

NOVELTY - Controlled release dosage composition comprises:

- (1) a solid dispersion comprising a low solubility drug dispersed in a cellulosic polymer and
- (2) an aqueous soluble cellulosic polymeric matrix containing the dispersion.

Most of the drug is amorphous.

DETAILED DESCRIPTION - INDEPENDENT CLAIMS are included for the following:

- (A) a controlled release dosage composition comprising an erodible polymeric matrix containing a solid dispersion comprising low solubility amorphous drug dispersed in an ionizable cellulosic polymer and
- (B) a controlled release dosage composition comprising an erodible polymeric matrix containing a solid dispersion comprising low solubility drug dispersed in an ionizable cellulosic polymer having alkylate and ester linked carboxylic acid substituents.

Most of the drug in (B) is amorphous.

USE - Used for treating diseases and disorders.

ADVANTAGE - The composition allows controlled delivery of the drug so that the concentration of drug in an in vitro or in vivo environment is increased and the bioavailability of the drug is increased. The time at which a maximum drug concentration in an in vitro or in vivo environment is obtained is delayed by 0.5-24 hours. Dwg.0/4

TECH.

drug comprises an antihypertensive, anxiolytic agent, anticlotting agent, blood glucose lowering agent, decongestant, antihistamine, antitussive, antiinflammatory, antipsychotic agent, cognitive enhancer,

\*\*\*cholesterol\*\*\* \*\*\*reducing\*\*\* agent, antiobesity agent, autoimmune disorders agent, hypnotic agent, anti-Parkinson's agent, antibiotic agent, antiviral agent, antiimpotence agent, antineoplastic, \*\*\*beta\*\*\* - \*\*\*blocker\*\*\* sedative, barbiturate, nutritional agent, , emetic, antiemetic, diuretic, anticoagulant, cardiotonic, androgen, corticoid, anabolic agent, antidepression agent, antiinfective agent, coronary vasodilator, carbonic anhydrase inhibitor, antifungal, antiprotoazoal,. . . agent comprises sildenafil. The blood glucose lowering agent comprises glipizide. The glycogen phosphorylase inhibitor comprises (R-(Rasterisk, Sasterisk))-5-chloro-N-(2-hydroxy-3-(methoxymethylamino) -3-oxo-1-(phenylmethyl)propyl)propyl)-1H-indole-2carboxamide or 5-chloro-1H-indole-2-carboxylic acid ((1S)-benzyl-3-(3R,4S)dihydroxypyrrolidin-1-yl)-(2R)-hydroxy-3-oxypropyl)amide. \*\*\*dosage\*\*\* form: The \*\*\*dosage\*\*\* form provides a Preferred maximum concentration of the drug in an aqueous in vitro test which is at least 1.5 times that obtained by an identical \*\*\*dosage\*\*\* composition containing the same amount of undispersed drug. When orally dosed, the \*\*\*dosage\*\*\* form provides a maximum concentration of drug in blood which is at least 1.25 times that obtained by an identical composition containing the same amount of undispersed drug. When orally \*\*\*dosage\*\*\* form provides an area under the blood drug concentration versus time plot of the drug which is at least 1.25 times \*\*\*dosage\*\*\* that obtained by an identical composition containing the same amount of undispersed drug.

TECHNOLOGY FOCUS - POLYMERS - The ionizable cellulosic polymer comprises hydroxyethylmethylcellulose acetate phthalate, . . .

L20 ANSWER 3 OF 6 DRUGU COPYRIGHT 2001 DERWENT INFORMATION LTD

ACCESSION NUMBER: 1990-06991 DRUGU PBTS

TITLE: Therapy of Hypercholesterolemia with HMG CoA Reductase

Inhibitors.

AUTHOR: Prager R

LOCATION: Vienna, Austria

SOURCE: ; WMWOA4; Wien.Med.Wochenschr. (139, Suppl. 105, 17-20, 1989)

2 Fig. 25 Ref.

AVAIL. OF DOC.: II, Medizinische Universitaetsklinik, Garnisongasse 13,

A-1090 Wien, Austria.

LANGUAGE: German

DOCUMENT TYPE: Journal

FIELD AVAIL.: AB; LA; CT

FILE SEGMENT: Literature •

AN 1990-06991 DRUGU P B T S

AB Use of HMG CoA reductase inhibitors in the therapy of hypercholesterolemias is reviewed, with reference to the mechanism of action and pharmacokinetics of inhibitors such as lovastatin (LV); practical use and indications for combined therapy with LV and drugs such as colestyramine: side effects of LV (including rhabdomyolysis when used in combination with other drugs) and contraindications. LV is effective in decreasing serum cholesterol in patients with both familial and

nonfamilial hyperlipidemias, and in type II diabetes. (congress). The only HMG CoA reductase inhibitor currently available for clinical use ABEX is LV. HMG CoA reductase inhibitors increase expression of LDL receptors (probably in the liver) and hence decrease LDL cholesterol and the risk of coronary heart disease. LV is metabolized to the corresponding beta-hydroxy acid and is excreted in the urine. Metabolism is not \*\*\*beta\*\*\* - \*\*\*blockers\*\*\* or digoxin. Combined affected by therapy with LV and colestyramine can decrease LDL cholesterol by 50-60%, and reduced \*\*\*dosage\*\*\* with LV is possible when used in \*\*\*Cholesterol\*\*\* combination. \*\*\*lowering\*\*\* effects of LV have been demonstrated in patients with familial combined hyperlipidemia, familial betalipoproteinemia, and nonfamilial hypercholesterolemia. LV also decreases VLDL and LDL cholesterol (and to a lesser extent triglycerides) in type II diabetics. Monotherapy with LV reversibly increases serum transaminases in 1-2% cases, but side effects are generally minor. However combination of LV with gemfibrozil, fibrozil analogs, lipid-decreasing doses of nicotinic acid, or cyclosporin-type immunosuppressives can cause rhabdomyolysis. Simvastatin and pravastatin are also mentioned. (S67/YC) (Therapie der Hyperlipidemie mit HMG CoA Reduktasehemmern.)

ABEX. . . disease. LV is metabolized to the corresponding beta-hydroxy acid and is excreted in the urine. Metabolism is not affected by \*\*\*beta\*\*\*

- \*\*\*blockers\*\*\* or digoxin. Combined therapy with LV and colestyramine can decrease LDL cholesterol by 50-60%, and reduced \*\*\*dosage\*\*\* with LV is possible when used in combination.

\*\*\*Cholesterol\*\*\* \*\*\*lowering\*\*\* effects of LV have been demonstrated in patients with familial combined hyperlipidemia, familial betalipoproteinemia, and nonfamilial hypercholesterolemia. LV also decreases. . .

L20 ANSWER 4 OF 6 EMBASE COPYRIGHT 2001 ELSEVIER SCI. B.V.

ACCESSION NUMBER: 2001027129 EMBASE

TITLE: Results of the low-dose (20 mg) pravastatin GISSI

Prevenzione trial in 4271 patients with recent myocardial

infarction: Do stopped trials contribute to overall

knowledge?.

AUTHOR: Marchioli R.

CORPORATE SOURCE: Dr. R. Marchioli, GISSI Prevenzione Coordinating Ctr.,

Consorzio Mario Negri Sud, Via Nazionale, 66030 S. Maria

Imbaro (CH), Italy. marchioli@cmns.mnegri.it
Italian Heart Journal, (2000) 1/12 (810-820).

Refs: 26

ISSN: 1129-471X CODEN: IHJOAM

COUNTRY: Italy

SOURCE:

DOCUMENT TYPE: Journal; Article

FILE SEGMENT: 018 Cardiovascular Diseases and Cardiovascular Surgery

037 Drug Literature Index 038 Adverse Reactions Titles

LANGUAGE: English SUMMARY LANGUAGE: English

AB Background. The aim of this study was to test the efficacy of a low-dose pravastatin regimen (20 mg daily) in patients with myocardial infarction. Methods. GISSI Prevenzione (GISSI-P) is an open trial on secondary coronary heart disease prevention: 4271 recent acute myocardial infarction patients (.ltoreq. 6 months) with total blood cholesterol .gtoreq. 200 mg/dl were randomized to low-dose \*\*\*cholesterol\*\*\* - \*\*\*lowering\*\*\* treatment (pravastatin 20 mg daily) or no treatment. GISSI-P was started in 1993 and its story was crossed by the publication of the results of similarly designed clinical trials. The publication of 4S results in 1994

Committee (SC) to change the protocol so that only patients whose total blood cholesterol was < 250 mg/dl could be randomized whilst patients with total blood cholesterol > 250 mg/dl who had already been enrolled in the study had to be re-evaluated and, if appropriate, pharmacologically treated. The DSMB and the SC agreed to stop randomization prematurely in late 1996 after the publication of CARE results. Results. Mean follow-up time was 23.0 .+-. 6.7 months (median 24.3 months). The two treatment groups were well matched at baseline. Pharmacological interventions recommended by the protocol were widely prescribed (antiplatelet agents > 90%, \*\*\*beta\*\*\* - \*\*\*blockers\*\*\* 42.7%, and ACE-inhibitors 40.2%). Mainly because of the on-course modification of the study protocol, 402/2133 (18.8%) patients in the control group started a \*\*\*cholesterol\*\*\* - \*\*\*lowering\*\*\* treatment during follow-up. Conversely, 296/2138 (13.8%) patients permanently stopped taking their tablets. Side effects, however, were the reason for discontinuing therapy in 57 (2.7%) patients in the pravastatin group, and patient reluctance to continue accounted for most of the remainder. After excluding control patients who had started a \*\*\*cholesterol\*\*\* - \*\*\*lowering\*\*\* treatment during follow-up, the following changes of median lipid concentrations in the control group over the whole course were observed: Total cholesterol -1.9%; LDL cholesterol -2.9%; triglycerides -2.0%; HDL cholesterol +1.4%. The analysis carried out excluding patients randomized to pravastatin treatment and actually not assuming the drug clearly \*\*\*cholesterol\*\*\* - \*\*\*lowering\*\*\* efficacy of low-dose pravastatin (total cholesterol -12.5%; LDL cholesterol -18.8%; triglycerides -7.9%; HDL cholesterol +3.4%). During the study 256 (6.0%) patients either died or had a non-fatal stroke or a myocardial infarction, 136 (6.4%) in the control group and 120 (5.6%) in the pravastatin group (relative risk 0.90, 95% confidence interval 0.71-1.15, p = 0.41); 160 patients died, 88 (4.1%) in the control group and 72 (3.4%) in the pravastatin group (relative risk 0.84, 94% confidence interval 0.61-1.14, p = 0.26). The few (n = 28) non-cardiovascular deaths were balanced: 16 (0.8%) in the control group and 15 (0.6%) in the pravastatin group. The reduction of cardiovascular events was more evident in the by-treatment analysis, with coronary heart disease deaths being significantly decreased (relative risk 0.60, 95% confidence interval 0.38-0.96, p = 0.04). The overall frequency of adverse events was similar in the two groups. No significant difference between treatment groups was found for total cases of cancer or at any particular site. Conclusions. Despite the decreased statistical power due to its premature stopping, the results of the GISSI-P suggest that a low-dose treatment with pravastatin (20 mg daily) is effective in reducing blood lipids, and underline the importance of long-term compliance with treatments in the search for a maximal effective \*\*\*dosage\*\*\* . Furthermore, the effects of a statin on total and coronary mortality quantified for the first time in a population exposed to Mediterranean dietary and lifestyle habits are markedly consistent with those obtained in different settings. (Ital Heart J 2000; 1 (12): 810-820). . . . 4271 recent acute myocardial infarction patients (.ltoreq. 6 months) with total blood cholesterol .gtoreq. 200 mg/dl were randomized to \*\*\*cholesterol\*\*\* - \*\*\*lowering\*\*\* treatment (pravastatin low-dose 20 mg daily) or no treatment. GISSI-P was started in 1993 and its story was crossed by the. . . treatment groups were well matched at baseline. Pharmacological interventions recommended by the protocol were widely prescribed (antiplatelet agents > 90%, \*\*\*beta\*\*\* - \*\*\*blockers\*\*\* 42.7%, and ACE-inhibitors 40.2%). Mainly because of the on-course modification of the study protocol, 402/2133 (18.8%) patients in the control group started a \*\*\*cholesterol\*\*\* - \*\*\*lowering\*\*\* treatment during follow-up. Conversely, 296/2138 (13.8%) patients permanently

prompted the Data Safety and Monitoring Board (DSMB) and the Steering

prescribed (antiplatelet agents > 90%, \*\*\*beta\*\*\* - \*\*\*blockers\*\*\*
42.7%, and ACE-inhibitors 40.2%). Mainly because of the on-course
modification of the study protocol, 402/2133 (18.8%) patients in the
control group started a \*\*\*cholesterol\*\*\* - \*\*\*lowering\*\*\* treatment
during follow-up. Conversely, 296/2138 (13.8%) patients permanently
stopped taking their tablets. Side effects, however, were the reason for
discontinuing. . . group, and patient reluctance to continue accounted
for most of the remainder. After excluding control patients who had
started a \*\*\*cholesterol\*\*\* - \*\*\*lowering\*\*\* treatment during
follow-up, the following changes of median lipid concentrations in the
control group over the whole course were observed: . . . +1.4%. The
analysis carried out excluding patients randomized to pravastatin
treatment and actually not assuming the drug clearly indicated the

\*\*\*cholesterol\*\*\* - \*\*\*lowering\*\*\* efficacy of low-dose pravastatin

(total cholesterol -12.5%; LDL cholesterol -18.8%; triglycerides -7.9%; HDL cholesterol +3.4%). During the study 256 (6.0%). . . in reducing blood lipids, and underline the importance of long-term compliance with

AΒ

treatments in the search for a maximal effective \*\*\*dosage\*\*\* . Furthermore, the effects of a statin on total and coronary mortality quantified for the first time in a population exposed. . .

L20 ANSWER 5 OF 6 PROMT COPYRIGHT 2001 Gale Group

ACCESSION NUMBER: 89:10589 PROMT

TITLE: 1989: Will FDA Open the Gates for New Drugs?

The pharmaceutical industry expects to see a shake up in

the cardiovascular market in 1989

SOURCE: Medical Marketing & Media, (Jan 1989) pp. 14-24.

ISSN: 0025-7354.

LANGUAGE: English

AB The pharmaceutical industry expects 1989 to see a shake up in the cardiovascular market, especially in the antihypertensive area.

\*\*\*Beta\*\*\* \*\*\*blockers\*\*\* will compete with new calcium channel blockers labeled for the treatment of hypertension, while the FDA is expected to soon approve of several second generation cardioselective ICI's Tenormin and Ciba-Geigy's Lopressor. In 1989, there will be new product introductions for \*\*\*cholesterol\*\*\* - \*\*\*lowering\*\*\* anti-infectives, 2 new classes of anti-ulcer drugs, nonsedating antihistamines, and a new antiarthritic agent. Many more new drug approvals are expected in 1989 than in 1988. The FDA had approved of only 7 new molecular entities in 1988, although the FDA did approve of a number of new \*\*\*dosage\*\*\* forms of FDA-approved drugs. New developments in the AIDS drugs market; cardiovascular indications' impact; the possible debut of a new generation of \*\*\*beta\*\*\* \*\*\*blockers\*\*\*; the consideration of erythropoietin for several disease states; some anti-infectives and antihistamines waiting for approval; and the FDA's possible moving on the backlog of NSAIDs are discussed. The pharmaceutical industry expects 1989 to see a shake up in the cardiovascular market, especially in the antihypertensive area.

L20 ANSWER 6 OF 6 USPATFULL

INVENTOR(S):

ACCESSION NUMBER: 1999:132893 USPATFULL

TITLE: Pharmaceutical preparations and medicaments for the

prevention and treatment of endothelial dysfunction

Noack, Eike Albrecht, Neuss, Germany, Federal Republic

of

Kojda, Georg, Koln, Germany, Federal Republic of

PATENT ASSIGNEE(S): ISIS PHARMA GmbH, Zwickau, Germany, Federal Republic of

(non-U.S. corporation)

PRIORITY INFORMATION: DE 1994-4410997 19940330 WO 1995-DE421 19950328

DOCUMENT TYPE: Utility

PRIMARY EXAMINER: Criares, Theodore J.

LEGAL REPRESENTATIVE: Marshall, O'Toole, Gerstein, Murray & Borun

NUMBER OF CLAIMS:

EXEMPLARY CLAIM: 1
LINE COUNT: 608

SUMM

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

The present invention describes the use of nitric-oxide-liberating or transferring compounds, stimulators of endogenous NO formation, as well as stimulators of guanylate cyclase, for prevention, treatment and elimination of endothelial dysfunctions and the diseases accompanying these dysfunctions or caused by them, as well as the use of said compounds to produce pharmaceutical products for the cited areas of application.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

\*\*\*Dosage\*\*\* occurs in the corresponding therapeutic doses, which are based on those in which the corresponding active principles are already used. . . much as 500 mg depending on the active ingredient. Daily doses of up to 350 mg are generally sufficient. The \*\*\*dosage\*\*\* and \*\*\*dosage\*\*\* range are to be chosen so that therapeutic plasma levels, which are as constant as possible are built up. The. . . individual active ingredients or in combination with each other or with known cardiovascular therapeutics, for example ACE inhibitors, antiatherosclerotics, antihypertensives, \*\*\*beta\*\*\* - \*\*\*blockers\*\*\*, \*\*\*cholesterol\*\*\* \*\*\*reducers\*\*\*, diuretics, calcium antagonists, coronary dilators, lipid reducers, peripheral vasodilators, thrombocyte aggregation inhibitors or other substances also used as cardiovascular therapeutics.